1-1-2002

Multiple-input, multiple-output modeling of the human thermoregulatory system

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Multiple-input, multiple-output modeling of the human thermoregulatory system

by

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A thesis submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Major: Statistics

Program of Study Committee:
Derrick Rollins, Major Professor
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Iowa State University

Ames, Iowa

2002

Graduate College
Iowa State University

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TABLE OF CONTENTS

CHAPTER 1. INTRODUCTION

1.1 GENERAL INTRODUCTION 1
1.2 INTRODUCTION TO THERMOREGULATORY MODELING OF THE HUMAN BODY 2
1.3 DESCRIPTION OF APPROACH 4
1.4 OBJECTIVE AND BACKGROUND OF THESIS 6
1.5 ORGANIZATION OF THESIS 6
1.6 REFERENCES 7

CHAPTER 2. LITERATURE REVIEW

2.1 INTRODUCTION TO MODELING OF A DYNAMIC PROCESS 9
2.2 HISTORY OF HUMAN THERMOREGULATORY MODELING 10
2.2.1 Empirical Approach 12
2.2.2 Analytical Approach 12
2.2.3 Computer-based Models 12
2.3 THE WISSLER PROGRAM 13
2.3.1 Energy Equations 16
2.3.1.1 Metabolic Energy Equation 17
2.3.1.2 Energy Equation for the Arterial Pool 19
2.3.1.3 Energy Equation for the Venous Pool 20
2.3.1.4 Heat Transport in the Lungs 21
2.3.1.5 Modification of Energy Equations 21
2.3.2 Mass Balance Equations 22
2.3.3 Control Equations 25
2.3.4 Summary of the Wissler Model 25
2.3.5 The Wissler computer program 26
2.4 CONTINUOUS-TIME HAMMERSTEIN MODELING AND H-BEST 29
2.4.1 The Exact Solution 31

2.5 SISO H-BEST APPLIED TO THE HUMAN THERMOREGULATION 33

2.6 SUMMARY OF CHAPTER 35

2.7 REFERENCES 36

CHAPTER 3. EFFECTIVE MIMO MODELING OF THE HUMAN THERMOREGULATORY SYSTEM

ABSTRACT 39

3.1 INTRODUCTION 40

3.2 H-BEST 42

3.3 EXPERIMENTAL MODELING APPROACH 44

3.4 RESULTS 51

3.5 CONCLUSION 53

3.6 REFERENCES 56

CHAPTER 4. ACCURATE PREDICTIVE MODELING WITH OPTIMAL EXPERIMENTAL DESIGN OF THE HUMAN THERMOREGULATORY SYSTEM

ABSTRACT 58

4.1 INTRODUCTION 59

4.2 EXACT SOLUTION TO A HAMMERSTEIN SYSTEM 61

4.3 EXPERIMENTAL MODELING APPROACH 64

4.3.1 H-BEST Algorithm 64

4.3.2 Optimizing the number of experimental trials 68

4.3.3 Optimizing the time length of experiments 74

4.4 RESULT 78

4.5 CONCLUSION 83

4.6 REFERENCES 85

CHAPTER 5. SUMMARY AND RECOMMENDATIONS FOR FUTURE WORK

5.1 CONCLUSIONS 87

5.2 FUTURE RESEARCH WORK 89

5.3 REFERENCES 90

APPENDIX A. FORTRAN COMPUTER CODE USED TO GENERATE THE TEST SEQUENCE FOR THE WISSLER PROGRAM 91

APPENDIX B. SAS COMPUTER CODE USED TO GENERATE THE D-OPTIMALITY DESIGNS FOR THE TWO RESPONSES 94

APPENDIX C. S-PLUS CODE USED TO COMPARE THE INFORMATION MATRIXES OF THE SEVEN RUN D-OPTIMAL DESIGN AND THE SIX RUN D-OPTIMAL DESIGN FOR SWEAT RATE. 100

APPENDIX D. S-PLUS CODE USED TO CALCULATE THE DETERMINANT OF THE NONLINEAR INFORMATION MATRIX FOR SKIN TEMPERATURE RESPONSE 102

APPENDIX E. S-PLUS CODE USED TO CALCULATE THE DETERMINANT OF THE NONLINEAR INFORMATION MATRIX FOR SWEAT RATE RESPONSE 105

ACKNOWLEDGMENTS 109

CHAPTER 1. INTRODUCTION

1.1. GENERAL INTRODUCTION

As mankind has started to work and explore in more environmentally hostile and extreme conditions, the need for understanding the human thermoregulatory system has increased. Specifically, when humans are exposed to extreme conditions it can affect our health. Thus, the importance of developing dynamic models for the human thermoregulatory system has increased. By modeling and simulating the human thermoregulatory system, it has become possible to study and predict the effect of these extreme environments on the human thermoregulation system. Accordingly, the ability to predict the intensity and extent of human limits in harsh environments can be of great use when planning workloads for jobs requiring exposure to extreme conditions.

There have been two main approaches to modeling the human thermoregulatory system. The two approaches can be categorized theoretical and empirical. The theoretical approach is based on the knowledge of science, while the empirical approach relies strongly on experimental data for model development. There are limitations to both of these approaches. The complexity and the lack of knowledge of the physiological behavior of the human body make the theoretical approach limited. In addition, data for the human thermoregulatory system are difficult to obtain. Therefore, the empirical approach, which requires a large amount of data, is impractical. Thus, the need to develop an accurate predictive model that requires a practical amount of data is of significant importance.

This work exploits a new solution developed for the modeling of engineering processes that can be described by the block-oriented Hammerstein system [6] that combines nonlinear static gains with linear dynamic systems. It is called the **H**ammerstein **B**lock-oriented **E**xact **S**olution **T**echnique (H-BEST) and was developed by Rollins et al. [11]. The H-BEST solution is a compact, continuous-time, solution that gives optimal (i.e., the smallest possible number) parameterization.

Hence, the main objective of this work is to develop an accurate and efficient predictive H-BEST model of the thermoregulatory system. More specifically, the approach that this work will take is to use H-BEST to predict skin temperature and sweat rate for changes in temperature, relative humidity, and wind speed by using the Wissler [14] program as a surrogate human. In addition, H-BEST will be used to optimize the number of experimental runs and reduce the experimental time for each run. Thus, this work also gives a practical procedure to model human subjects.

After reviewing literature in the field of human thermoregulatory modeling, we could not find any studies that develop a block-oriented closed form model of the human thermoregulatory system from a small amount of experimental trials. Hence, this work takes a new approach in developing accurate and practical models for human thermoregulatory system.

1.2. Introduction to Thermoregulatory modeling of the Human Body

As stated earlier, the need to model the human thermoregulatory system has become of great importance. Hence, extensive research has been done to develop models that will accurately predict bodily thermoprocesses and estimate environmental effects on these processes. This section presents a short introduction to modeling the human thermoregulatory system and the physiological mechanisms that are involved in thermoregulation.

There are four different physiological mechanisms in the body used to regulate temperature: vasodilation, vasoconstriction, shivering, and sweating. Vasodilation is the mechanism in which the blood flow rate to the skin is increased. As a result the skin temperature is increased. By the reverse mechanism, vasoconstriction, the blood flow rate is decreased to the skin, thereby decreasing the skin temperature. Furthermore, shivering and sweating can also regulate the body temperature. Shivering leads to increased metabolic conversion in the muscles and thereby stimulates an increase in body temperature. Since the efficiency of shivering in muscles is relatively low, about 10-15% [12], considerable energy is converted to heat, which is used to increase the body temperature. In addition, the body can decrease its temperature by sweating, and the surface heat loss is then regulated by the amount of evaporation.

There are various models developed for the modeling of the human thermoregulatory system. These models vary significantly in the way they segment the body as well as in mathematical detail and empirical parameters used. As stated, the two main approaches to modeling the human thermoregulatory system are the empirical approach, and the theoretical approach. The empirical approach is done mainly by experiments with curve-fitting data. The theoretical approach uses first principles understanding to explain the behavior of the human thermoregulatory system.

Obtaining data from human subjects when modeling the human thermoregulatory system can be both costly and in some situations inhumane. Thus, computer programs are often used to simulate the thermoprocesses in the body for different environmental conditions. That is, computer-based models are used to generate the responses for different inputs due to the complexity and difficulty of obtaining thermoregulatory data from a real person. There are a great number of factors that can be considered in thermoregulation for example: height, mass, individual's physical fitness (oxygen consumption), air temperature, level of acclimation, wind speed, relative humidity, exercising level, individual's age, and gender.

1.3. Description of Approach

As stated earlier, the main objective of this work is to successfully and practically model the thermoregulatory system by using H-BEST. The approach taken in this work is to model data simulated by the Wissler model [14] for a multiple-input, multiple-output (MIMO) study of the human thermoregulatory system. More specifically, this work focuses on developing accurate and efficient H-BEST models for the skin temperature and sweat rate for changes in ambient temperature, relative humidity, and wind speed. For this study, Statistical Design of Experiments (SDOE) is used to optimize the information content of the experimental data. That is, the optimization is based on generating as few runs as possible, while obtaining accurate estimates of the model parameters.

In addition, the H-BEST solution is used to further reduce the number of experimental trials and the experimental time for each experimental trial. That is, the optimization of number of experimental runs and the minimization of the experimental time required for model identification are obtained by using the H-BEST closed-form solution with the D-optimal criterion [1]. Hence, this work seeks to obtain insight of practical importance to model real human subjects.

There were various preliminary challenges faced for this study that had to be overcome before proceeding. These include the lack of a steady state for response variables, performing an enormous number of experiments, and time required to run each experiment on the computer. The following part of this section will include a short description of each limitation and the approach taken to overcome these limitations.

First, the simulated response curves never reached steady state but tend to level off and oscillate after a while. Since the experiment, for time limitations, cannot be carried out for hours after each input change, the experiments were stopped after an appropriate time when the response curves started to level off. Second, a large number of experiments are usually a problem when investigating a MIMO system with all main effects and interactions. To do a total investigation of all the interactions of the inputs, a full factorial experiment has to be carried out. For example, with five inputs, each at two levels, $2^5 = 32$ experiments are required. By using SDOE the number of required runs can be reduced significantly, while maintaining an ability to test for main effects and critical interaction effects.

Finally, one problem was that the running time of each experiment was too long. Most models of the human thermoregulatory system are computer-based. The original Wissler model is written in FORTRAN code and was run on a Macintosh PowerBook 180. The time for each experimental run on the Macintosh computer was relatively long, approximately 45 minutes. Hence, there was a need to decrease the running time. Therefore, to increase speed and to use accessible computers it was necessary to modify the original FORTRAN code to run on a IBM Personal Computer (PC) format. The computer program was converted to a 450 MHz PC platform by completing the work initiated by Erickson [5] and the time for each run was at least 10 times faster on the 450 MHz Pentium II than on the Macintosh.

1.4. Objective and Background of Thesis

The overall objective of this thesis is to develop an accurate and practical block-oriented dynamic model for a MIMO case of the thermoregulatory system. The method used by this work is H-BEST. The data are obtained from Wissler's model acting as a surrogate person. As stated earlier, the practicality of the H-BEST is maintained by using SDOE, which will reduce the number of required runs, while still maintaining a high accuracy in parameter estimates. In addition, the H-BEST model is used to even further minimize the required amount of experimental runs while still obtaining an accurate predictive model of the human thermoregulatory system. Furthermore, the performance of the H-BEST model with respect to length of experimental time is also investigated by using the D-optimal criterion.

The motivation for this study came from the work of Walker [13]. Walker accurately modeled the human thermoregulatory system, simulated by the Wissler model, with H-BEST for a single-input, single-output (SISO) process. The study showed that H-BEST could accurately predict the response. As stated earlier, H-BEST is an exact solution to a Hammerstein process and hence, can predict well for processes that are Hammerstein or approximately Hammerstein in nature. Following the success of Walker [13], the next step was to extend the work to modeling a MIMO process of the human thermoregulatory system with H-BEST.

1.5. Organization of Thesis

To achieve our objective, the thesis is organized in the following manner. Chapter 2 is a literature review of the approaches to thermoregulatory modeling. The first section of this chapter describes both empirical and theoretical methods used for modeling the human thermoregulatory system and their limitations. Chapter 2 also consists of a detailed description of the Wissler model [14] and the SISO study of the human thermoregulatory system by Walker [13]. In the last section of Chapter 2, a detailed presentation of H-BEST is included. Chapter 3 describes a successful study of H-BEST MIMO of the human thermoregulatory system. Chapter 4 describes a study to optimize the number of experimental trials and total experimental time. Finally, Chapter 5 includes general conclusions as well as potential future research.

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CHAPTER 2. LITERATURE REVIEW

2.1 INTRODUCTION TO MODELING OF A DYNAMIC PROCESS:

As stated earlier, the need to understand and model the human thermoregulatory system has become of greater interest and importance. This is especially due to industrial developments where mankind is starting to explore and work in more environmentally hostile conditions. There are two main approaches used to model the thermoregulatory system -- the theoretical and empirical approach. Theoretical models are derived from the fundamental laws of science. In contrast, empirical models strongly rely on experimental data and their model coefficients do not usually have physical meaning. There are various limitations that have to be considered when using these modeling approaches. Empirical models, such as linear regression and artificial neural network, rely strictly on experimental data to obtain the fitted model. These models are limited in two ways. First, the data collected can give an incomplete image of the whole picture. That is, the data set is plotted and an equation is derived from the response. Thus, the equation holds true for this data set, but the response behavior may change outside the fitted input space (i.e., when extrapolating). Hence, the data are limited to the conditions set at the experiment. Consequently, the practical use of the model will be limited, since the model might only be valid for those specific and rare conditions. Another limitation with empirical methods is the requirement of constant sampling rate. Also, the dynamic empirical modeling methods are limited to only predicting responses in discrete-time not continuous-time. For the theoretical models, which rely on theory using biology and the laws of physics to derive equations, it can be hard to achieve the knowledge necessary to understand the dynamic process behaviors and therefore hard to derive these models. As a result, many processes cannot be modeled theoretically because they are too complex.

As stated earlier, it is important to study the strain on humans in different environments. However, it is unethical to do experimental studies in critical situations where the body is exposed to extreme cold or heat. Hence, because of the difficulties of collecting experimental data safely, computer programs are often used instead of human subjects for experimentation on the thermoregulatory system. The computer programs apply the laws of physics to calculate the desired outputs by using various heat and mass transfer equations describing processes in the human body. These computer programs have been contributing to a deeper understanding of the principles of human thermoregulation. That is, the computer models can serve as research tools for human performance, thermal acceptability, temperature sensation, clinical and therapeutic treatments, safety limits especially for the car industry or military applications.

This chapter will start with discussing the history of modeling of the human thermoregulatory system. That is, describe different empirical and theoretical models developed. However, this chapter will focus on the computer program, called Wissler that is used as a surrogate human for this study. The modeling approach used in this study called H-BEST is also widely described in this chapter.

2.2 History of Human Thermoregulatory Modeling

There are many different approaches to model human thermoregulation. These models differ by assumptions made in the mathematical formulation, performance criteria, and selection of the process representation. The importance of understanding human thermoregulation has increased during the last century. More specifically, in the history of human thermoregulatory modeling, models have been developed dating back to the late 1960's. These models vary significantly in the way they segment the body. Some models used lumped parameters while others used finite difference to model the components. They also vary in detail and empirical parameters used. Models like Wissler [36], Fiala [12], Stolwijk [30], Gordon et al. [16], and Gagge et al. [14], apply the basic concepts of heat transfer, the relationship of transfer of thermal energy by conduction, convection, and evaporation to the human body. The models vary in complexity of development of both the physiological details and the mathematical computations. However, in their development, these models do not take into account individual variability. Consequently, this simplifies the development of the model, but also limits the effectiveness of modeling for individual factors.

Two different paths have been taken to understand the thermoregulatory system. The first path is the empirical approach. This path concentrates on understanding the processes involved and using experimental data. The second one is a theoretical path, also called the analytical approach. This research approach uses fundamental knowledge of the physical and biological processes of the thermoregulatory system to describe the mechanism responsible for controlling thermoregulation. The following part of this section will describe the empirical approach and the theoretical approach to modeling the human thermoregulatory system.

2.2.1 Empirical Approach.

The goal of the empirical approach is to develop an understanding of the physiological processes that the body uses in regulating the temperature. This approach is based mainly on curve fitting data or empirical modeling. Thus, this approach works well for individual cases but cannot necessarily be applied when extrapolated to other cases. Benzinger [5] and Fusco [13] are two of the derived models used in the field of empirical approach to thermoregulation of human body.

2.2.2 Theoretical Approach

The theoretical thermoregulatory models are developed to study human performance with different environmental stresses. These models are developed using the principles of thermodynamics, heat transfer and mass transfer equations, and other areas supporting a theoretical approach. The models developed from the engineering perspective may vary in many ways. The number of sections that the body is divided into and how those sections are represented are two critical manners in which they differ. They also vary in complexity of development of both the physiological and mathematical computation. Some of the most notable models developed by the theoretical approach are the Gagge [14], Gordon [16], NASA 41 Node Model [6], Stoljwijk [30], Werner [33], Fiala[12], and Wissler [36] models.

2.2.3 Computer-based Models

In this study, two different computer programs were used to simulate the data. Professor Eugene H. Wissler, at the University of Texas in Austin, designed one of these computer programs. In the Wissler [36] program, equations are constructed for the various thermal processes of the human body. As for most of the computer programs constructed for the thermoregulatory system, the processes can be described by the laws of physics. However, there are some processes that cannot be defined by those equations and in that case experimental data are used. Hence, the Wissler model is actually semi-theoretical.

The second computer program used in this work was developed by Dr Dusan Fiala [12], at the Institute of Energy & Sustainable Development, De Montfort University, UK. This program is also a semi-theoretical program. That is, most of the equations for the thermoregulatory model are based on laws of physics. However, some of the processes of the thermoregulatory model are described by equations developed from experimental data. Unfortunately, the Fiala model did not turn out to be a useful source of the simulation data, because of the lack of stability in reaching steady state for the chosen initial and experimental conditions. Hence, only the Wissler program is used as a surrogate human for this study. The following section describes the Wissler program in detail.

2.3 The Wissler Program

Predicting human thermoregulation under a variety of circumstances is very important when dealing with problems encountered by people exposed to extreme environments. One of the most important concerns for the human body in environmentally hostile conditions is the regulation of temperature. There are several mechanisms and factors employed in modeling the human thermoregulation. These factors include room temperature, relative humidity, exercise level, duration of exposure, clothing, age, level of physical fitness, acclimation, gender, weight, and surface area. All of these factors can affect the skin temperature and the core temperature, which determines the actions taken by the body. For example, in a hot environment the body increases the rate at which thermal energy is removed from the body through the use of evaporation of sweat from the surface of the skin. However, in cold temperature, the body can generate thermal energy from metabolic reactions through shivering. Hence, to adequately interpret temperature profiles for a thermal model, which is applied to situations involving both heat and cold stress, we must account for the following physical factors:

1. *Local generation of heat by metabolic reactions*
2. *Conduction of heat due to thermal gradients*
3. *Convection of heat by circulating blood*
4. *The geometry of the body*
5. *The existence of an insulating layer of fat and skin*
6. *Countercurrent heat exchange between adjacent large arteries and veins*
7. *Heat loss through the respiratory tract*
8. *Sweating*
9. *Shivering*
10. *Storage of heat*
11. *Environmental conditions such as temperature, wind speed, and relative humidity.*
12. *Clothing*

Some of these factors, such as environmental conditions, are easy to measure. On the other hand, a factor such as the local rate of heat generation is difficult to measure, and its values must be deduced from indirect measurement. One of the principal uses of a mathematical model is to assign reasonable values to those parameters, which cannot be measured directly in the experiment.

In the Wissler model the body is divided into 15 cylindrical regions, which are the head, thorax, abdomen, and the proximal, medial, and distal segments of both arms and legs. A schematic figure of the body is shown in the Fig. 2.1 below.

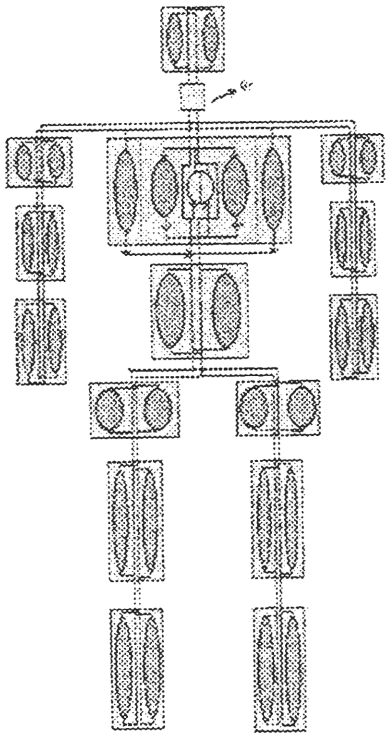

Figure 2.1: Schematic of the human body as used in the Wissler [37] model.

Each of the 15 elements consists of a combination of tissue, bone, fat, and skin. In addition, each element has a vascular system, which can be divided into three subsystems representing the arteries, veins, and capillaries. The circulatory path is faithfully reproduced in the sense that a tracer material introduced into an artery will flow both into the capillaries of that segment and into the arteries of more distal segments. Blood leaving the capillaries flows into veins where it is mixed with venous blood from more distal segments. The mixed venous stream at the heart flows into the pulmonary artery, the blood returns to the left side of the heart. Exchange of both mass and heat occurs in the lungs.

Within a given segment in the Wissler model, variables may depend on both radial position and time. Some quantities, such as density and specific heat, do not depend on time; but many others, including temperature, O_2 tension, metabolic rate, and blood perfusion rate, depend on both position and time. Some of these variables, such as the perfusion rate and metabolic rate are defined by physiological control equations. Others, such as temperature and O_2 tension, are dependent variables whose immediate values depend on the previous history of the subject.

For better understanding of this whole-body model a description of the energy equations, mass balances, and control equations is given in this chapter. This model also consists of equilibrium relationships, which are the dissociation curves of CO_2 and O_2, calorific oxygen equivalent, and respiratory quotient. The oxygen dissociation equation and carbon dioxide buffer equations used in this model are developed by Grodins et al. [17]. The respiratory quotient represents the molar ratio of CO_2 production to O_2 consumption. The calorific oxygen equivalent statement relates the metabolism of O_2 to energy metabolism in terms of respiratory quotient.

2.3.1. Energy Equations

The Wissler [36] model is one of the most complete semi-theoretical models of the thermoregulation in existence at the present time. Accordingly, the theoretical component of the Wissler model is based on the energy balances for metabolism, energy balance in the arterial pool and the venous pool, and sensible and insensible heat loss in respiration. The model is modified and simplified with assumptions in some of the elements to be able to describe the complex processes of the human body. The arterial pool is modified to account for the presence of large arteries in the thoracic section and the venous pool is modified in the abdominal and thoracic sections to account for the presence of large veins. The model of the vascular system is quite detailed, including arteries, veins, and capillary beds. It allows for cooling of the blood as it moves from distal to the heart and accounts for counter-current heat transfer between the veins and arteries.

The general energy equation balance for the human thermal system is

$$\dot{Q}_{st} = \dot{Q}_m \pm \dot{Q}_c \pm \dot{Q}_r - \dot{Q}_e \pm \dot{Q}_k \pm \dot{Q}_{res} \tag{2.1}$$

where $\dot{Q}_{st}$ is the rate of storage of heat; $\dot{Q}_m$ is the metabolic energy rate; $\dot{Q}_c$ is the convective surface energy gain/loss rate; $\dot{Q}_r$ is the radiative heat gain/loss rate; $\dot{Q}_e$ is the rate of evaporative energy loss; $\dot{Q}_k$ is the rate of conductive heat gain/loss; and $\dot{Q}_{res}$ symbolizes the rate of heat loss/gain through the respiratory tract. Thus, the energy equations for the body follow this general energy Eq. 2.1. There are five main energy balances that provide the foundation for the Wissler model. These energy equations are the metabolic energy equation, the energy equation for the arterial and the venous pool and the energy equations for the lungs. These energy equations will be described individually in the following subsections.

2.3.1.1 Metabolic energy equation

The heat that is generated by the metabolic equations is either stored in the element (i.e., one of the 15 cylindrical regions of the body), carried away by circulating blood, or conducted to the surface, where it is transferred to the environment. This is simply a statement of the first law of thermodynamics, which can be mathematically formulated as the heat conduction Eq. 2.2 below.

$$\rho_i c_i \frac{\partial T_i}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}\left(k_i r \frac{\partial T_i}{\partial r}\right) + q_{mi} + \rho_b c_b \omega_{bi}(T_{ai} - T_i)$$

$$+ h_{ai}(T_{ai} - T_i) + h_{vi}(T_{vi} - T_i) \qquad (2.2)$$

where T_i(t, r) is the instantaneous temperature of the tissue, bone or viscera at a distance r from the axis of the ith element; ρ_i(r) and ρ_b symbolizes the density of tissue and the density of blood; c_i(r) and c_b is the specific heat of tissue and blood, respectively; k_i(r) is the thermal conductivity of tissue; q_{mi}(t, r) is the metabolic heat generation rate per unit volume; ω_{bi}(t, r) is the volumetric flow rate of blood entering the capillary beds per unit volume; h_{ai}(t, r) and h_{vi}(t, r) are the heat transfer coefficients between the arteries and the tissue per unit volume and heat transfer coefficient between the veins and the tissue per unit volume, and T_{ai}(t, r) and T_{vi}(t, r) represent the temperature of arterial blood in the ith element and the temperature of venous blood in the ith element

The term on the left-hand side of Eq. 2.2 is the rate of accumulation of thermal energy per unit volume due to the changing temperature of the tissue and capillary blood in the volume. This equals the sum of the five terms on the right-hand side. The five terms represent in order: the net rate of conduction of heat into a unit volume, the rate of heat generation by metabolic reactions, the net rate at which heat is carried into the volume by capillary blood, the rate at which heat is transferred from arterial blood to the tissue, and the rate at which heat is transferred from venous blood to the tissue.

This energy equation is based on a few assumptions to simplify the modeling. First, it should be observed that this form of heat conduction equation is applicable only to an axially symmetrical system in which the longitudinal conduction of heat transfer is negligible. This means that the analysis does not apply to situations in which the subject is curled up in a ball in order to conserve heat. If the subject is moving so that there is a uniform flow of air around each of the elements, the analysis should apply. Accordingly, neglecting longitudinal conduction should only introduce a relatively small error in long thin elements such as the arms and legs and in the trunk, which is relatively well insulated at the ends. However, the error may be quite large in the head.

Secondly, it is also assumed that there is perfect mixing between blood in the capillaries and neighboring tissue. That is, the temperature leaving a capillary bed is equal to the temperature of the neighboring tissue. Finally, it is assumed that the rate of heat transfer from blood in large vessels to the neighboring tissue is proportional to the difference between the blood and the tissue temperatures. Thus, h_a and h_v represent the heat exchange coefficients for the arteries and veins, respectively.

2.3.1.2 Energy Equation for the Arterial Pool

When formulating the equation for the energy balance for the arterial pool it is assumed that the arteries in the *i*th element form a pool having a uniform temperature, T_{ai}. The rate of accumulation of thermal energy in this reservoir is equal to the sum of the net rate at which heat is carried in to the pool by flowing blood, the rate at which heat is transferred from neighboring tissue to blood in the pool and the rate at which heat is transferred directly from the venous pool to the arterial pool due to the proximity of certain arteries and veins. This is expressed mathematically in Eq. 2.3 below.

$$m_{ai} c_b \frac{dT_{ai}}{dt} = \rho_b c_b W_{ai}(T_{am} - T_{ai}) + 2 l_i \pi \int_0^{ai} h_{ai}(T_i - T_{ai}) r dr + H_{avi}(T_{vi} - T_{ai}) \qquad (2.3)$$

where T_{am}(t) is the temperature of blood entering the arterial pool of the ith element from the mth element; ρ_b is the density of blood; c_b is the specific heat of blood; m_{ai} is the mass of blood contained in the arterial pool of the ith element; W_{ai} is the volumetric flow rate of blood entering the arterial pool of the ith element; l_i is the length of the ith element; and H_{ai} is the heat transfer coefficient for direct transfer between large veins and arteries. The integral is necessary in Eq. 2.3 because tissue temperature is a function of r.

2.3.1.3 Energy Equation for the Venous Pool

The equation is based on the same assumptions and theory as for the arterial pool, but this time applied to the venous pool in each segment. The energy equation for the venous pool is expressed mathematically by the following Eq. 2.4:

$$m_{vi} c_b \frac{dT_{vi}}{dt} = \rho_b c_b W_{vi}(T_{vn} - T_{vi}) + 2 l_i \pi \int_0^{ai} (\rho_b c_b W_{vi} + h_{vi}) \times (T_i - T_{vi}) r dr + H_{avi}(T_{ai} - T_{vi}) \qquad (2.4)$$

where T_{vn}(t) is the temperature of blood entering the venous pool of the ith element from the nth element; ρ_b is the density of blood and c_b is the specific heat of blood; m_{vi} symbolizes the mass of blood contained in the venous pool of the ith element; W_{vi} represents the volumetric flow rate of blood entering the venous pool of the element; l_i is the length of the ith element; and H_{avi} is the heat transfer coefficient for direct transfer between large veins and arteries.

2.3.1.4 Heat Transport in the Lungs

The lungs are assumed to be a well-mixed region of constant volume, V_L. The gas passes through the lungs at a constant rate, V_{ex}. The expired air is saturated with vapor at the temperature of the respiratory tract, T_{res}, since heat and water vapor are transferred with ease in the lungs. The rate which sensible heat is lost through the respiratory tract is described by the following Eq. 2.5:

$$\dot{Q}_{res} = \dot{V}_{ex}\,\rho_g\,c_p\,(T_{res} - T_{in}) \qquad (2.5)$$

where T_{in} is the temperature of the inspired air. The equation for insensible heat loss due to respiration is expressed mathematically by Eq. 2.6 as follows:

$$\dot{Q}_{res} = \dot{V}_{ex}\frac{\tilde{h}_{fg}}{22{,}4}\cdot\frac{p_{H_2O} - p_{H_2O,i}}{760}\,\frac{273}{273 - T} \qquad (2.6)$$

where $\tilde{h}_{fg}$ is the molar latent heat of vaporization of water.

2.3.1.5 Modification of Energy Equations

The conditions for each element in the body differ and therefore, the energy equation in this element needs to be modified. Accordingly, the equations for the venous temperature is slightly modified in the abdominal section because the temperature there is different than in Eq. 2.4 due to the two veins, one from each leg, flow into this section. It is also necessary to modify the equation for the thoracic section because all venous streams terminate and all arterial streams originate in this section. It is assumed that the temperature of blood entering the pulmonary capillaries is equal to the mean temperature of venous streams entering the right ventricle. This causes a modification in the metabolic energy equation because the temperature of the venous blood entering the pulmonary capillaries is different from the temperature of the arterial blood entering more superficial capillaries of the thorax. The venous and arterial energy equation must be modified to take into account the fact that mixed venous blood flows through the pulmonary artery into the pulmonary capillaries, which in turn empty into the thoracic arterial pool. When modifying the energy equation for the venous pool assumptions need to be made about the rate at which heat is transferred from venous blood in the thorax at air in the respiratory tract. Furthermore, it is assumed that the total rate of heat loss through the respiratory tract depends on the ventilation rate and the temperature and humidity of inspired air. It is assumed that 25% of the heat loss through the respiratory tract comes from the arterial pool in the head 25% from the venous pool in the head, and 50% from the venous pool in the thorax.

2.3.2 Mass balances in the Lungs

Although the Wissler model is primarily a thermal model, it also contains mass balances equations for oxygen, carbon dioxide, and lactic acid in order to provide information required in the control equations for perfusion and ventilation. In order to evaluate chemical factors, which are included in the model, it is necessary to construct material balances for the principal reactants and products in the metabolic reactions. These reactions are very complex since the substrate can be either carbohydrate or fat, and the products may be carbon dioxide and water, or lactic acid, depending on the availability of oxygen in tissue. Readers who are interested in a detailed discussion of these reactions should refer to a standard biochemistry textbook, for example see [8] or [34].

Equations in this model are based on a greatly simplified metabolic scheme that, nevertheless, includes most of the essential features. It is assumed that energy is obtained from the oxidation of carbohydrate, which can be represented by glucose. The objective of metabolic reactions involved in exercise is to form adenosine triphosphate (ATP), a high-energy compound. ATP is readily hydrolyzed in the muscle cells, ultimately providing energy to do mechanical work. It is also assumed in this model that the level of exercise determines the rate of production of ATP.

Two equations of importance are the equations of change of oxygen concentration since they are used in the control equations in the Wissler model. In developing equations of oxygen change for large arteries and veins, it is assumed that there is neither reaction nor exchange of mass with surrounding tissue. Hence, the following equation expresses the oxygen balance for the arterial pool

$$V_{ai}\frac{dC_{aO_2,i}}{dt} = W_{ai}(C_{aO_2,m} - C_{aO_2,i}) \qquad (2.7)$$

where $C_{aO_2,i}$ is the oxygen concentration of arterial blood in the ith segment; $C_{aO_2,m}$ is the oxygen concentration of blood entering the arterial pool; and V_{ai} is the volume of the arterial pool in the ith segment. The corresponding equation for oxygen balance for the venous pool is

$$V_{vi}\frac{dC_{vO_2,i}}{dt} = W_{vi}(C_{vO_2,m} - C_{vO_2,i}) + 2l_i\pi\int_0^{a_i}\omega_{bi}(C_{vO_2,m} - C_{vO_2,i})r\partial r \qquad (2.8)$$

where W_{vi} is the volumetric flow rate for venous blood entering the ith element from the mth element; and the $C_{vO_2,m}$ under the integral refers to the oxygen concentration of blood flowing into the venous pool from capillaries of the element.

Another important mass balance equation used for the control equations in the model is the equation for change of oxygen in the lungs. When deriving this equation the following assumptions are made. First, the blood volume in the lungs is neglected. Secondly, the partial pressure of each component in the alveolar component is equal to the tension of that gas in blood as it leaves the pulmonary capillary. Thirdly, 2% of the pulmonary blood flow is shunted across the pulmonary capillary without gas exchange. The oxygen balance for the lungs is

$$V_L \frac{dp_{O_2}}{dt} = 760\, N_{baO_2} + \dot{V}_{ex}(\, p_{O_2 in} - p_{O_2 ex}\,) \tag{2.9}$$

where $p_{O_2,in}$ and $p_{O_2,ex}$ are the partial pressure of oxygen in inspired and expired gas; the numerical factor 760 appears because gas concentration in blood is measured in milliliters of dry gas at STP per milliliter of blood; N_{baO_2} represents the rate of exchange of oxygen between blood and alveoli per unit volume; and V_{ex} is the volumetric rate of the expired gas.

Corresponding equations can be written for CO_2 and non-respiratory gases by changing the subscript designating the gas. Equations of change are required also for lactate, which is produced during anaerobic glycolysis. In this case, it is assumed that lactate is transferred from muscle to blood at a finite rate which is proportional to the difference in concentration.

The general and most important mass balances for this model were given in this section. In the same manner as the energy equations are modified, the mass balance equations for this model are also modified for different bodily regions. As an example, in the lungs the exchange of gas between pulmonary and capillaries and the alveolar space has to be taken into account.

2.3.3. Control Equations

The mass balances given above (i.e., Eqs. 2.7, 2.8, and 2.9) permit one to compute temperature and chemical species concentrations when physiological parameters, such as local metabolic rates, tissue perfusion rates, and the ventilation rate, are known. Thus, the Wissler model also consists of control equations for perfusion, shivering and sweating. The following section is a short description of these control equations.

The control function for perfusion is based on the knowledge that for regulation of central temperature, the rate at which blood perfuses the skin can be controlled. Hence, as body temperature rises, blood flow to the skin increases, thereby increasing the skin temperature and the rate of heat transfer to the environment. Furthermore, the control function used for sweating is a linear relationship between the sweat rate and the increase in central and mean skin temperature. That is, the sweating rates in each section are weighted for the density of sweat glands. Likewise, the control equation for shivering can be described either as a first-order dynamic model or as a fading memory model. These dynamic models are equivalent, except for a slight difference in behavior during periods of rapidly diminishing cold stress. Additionally, the shivering equation accounts for the relationship between the skin and core temperature and their rates of change.

2.3.4 Summary of the Wissler Model

The Wissler [36] model is one of the most complete semi-theoretical models of the thermoregulation in existence at present. According to Fig. 2.1, the body is divided into 15 cylindrical regions in the Wissler model. The whole-body model consists of energy equations, mass balances, equilibrium relationships, and control equations, which are all used for computation in each of the 15 elements of the body. Fig. 2.2 below shows a schematic picture of how these relationships and equations are all integrated together to form the coupled model. Environment and exercise effects also influence the functioning of this system of equations.

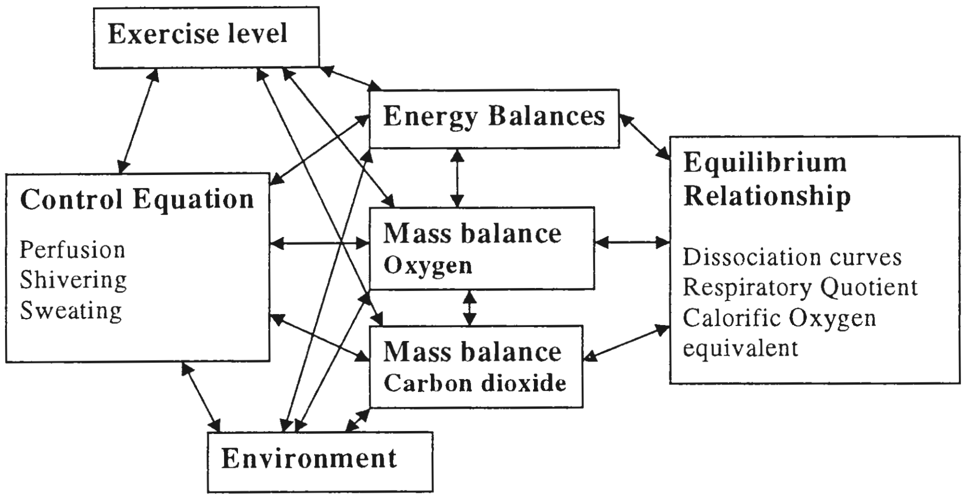

Figure 2.2: Schematic of equations and relationships used in the Wissler model.

As stated earlier, the Wissler program is a computer-based model. Thus, the next section of the chapter will describe the Wissler computer program in further detail. Specifically, the input files and output files used for this study is discussed.

2.3.5. The Wissler computer program

The Wissler model is chosen to generate the simulated data for this study for several reasons. The model is well known and has been used for several studies. In addition, these studies have also shown that the model is robust. Secondly, the program is based on a platform that is reasonably accessible, allowing for it to be used without rewriting and updating the code. There is only need to specify the physical parameters in the input files. Thirdly, the accuracy of the code can be tested against known simulation results that have been previously verified. Fourthly, the program has also been under the direction of a single person for the entire development process.

The Wissler program has been developed with several purposes in mind. One is to provide a theoretical framework for understanding human response to exercise under various environmental conditions, and another is to provide a rational basis for predicting human response to exercise in these various environments. Clearly, the second objective depends on the first. Even though the understanding of many physiological phenomena remains incomplete, this model seems to be sufficient to allow the use of modeling for cautious predicting of the human response to a variety of stressful conditions. Hence, the Wissler model covers the full range of human experience extending from immersion in cold water to exercise in a hot humid environment. As a result, this model has been used successfully to analyze the performance of divers working as deep as 450 meters.

The Wissler program is originally written in FORTRAN 77 source code for a Macintosh PowerBook 180. To increase speed and to use accessible computers, without losing any information and still obtaining the same results with both computer platforms, a significant goal of this work was to modify the original FORTRAN code to run on an IBM compatible Personal Computer (PC). The computer program was converted to a PC platform by completing the work initiated by Erickson [9] and the speed for each run was then at least 10 times faster on the PC than on the Macintosh.

The Wissler computer program consists of the FORTRAN source code and a few associated files. The FORTRAN source code is the heart of the program consisting of all the mass and heat transfer calculations. The associated files are the input files, which specify the environmental and physical conditions for each experiment, and also associated files that consist of physiological data for the environment and human thermoregulatory responses. There are a number of variables that needs to be specified in the input file and they are all listed below.

1. *Subject's weight and mean skinfold thickness, or regional subcutaneous fat thickness*
2. *Thermal resistance and permeability for water vapor of the clothing on each bodily element*
3. *Resting and total metabolic rates (exclusive of shivering)*
4. *Environmental conditions, including the dry-bulb temperature, humidity, radiant flux, and wind speed for a gas, or temperature and fluid speed for a liquid.*

Each time the Wissler program is executed an output file is created, which consists of different output data. The various output data generated by the Wissler program is listed below.

1. *Temperature at 15 radial points within each of the 15 bodily elements,*
2. *Arterial and venous blood temperatures in each element,*
3. *Local perfusion rate at each radial node,*
4. *Metabolic rate at each node owing to resting metabolism, exercise, and shivering*
5. *Oxygen, carbon dioxide, and lactate concentration in tissue and blood at each radial node.*
6. *Regional rates of sweat production.*
7. *Rate of sweat evaporation, which may be less than the rate of sweat secretion.*
8. *Ventilation rate.*
9. *Temperature at up to 6 additional radial points within clothing.*
10. *Amount of accumulated sweat at each clothing node.*
11. *Rate of heat transfer between exposed surfaces and the environment owing to convection and radiation*

In addition to the output file, the Wissler program generates a summary file that consists of a summary table, which is also found at the end of the output file. The summary table consists of the core, mean skin, arterial, chest, abdomen, head, thigh, calf, biceps, and forearm temperatures at each specified time interval.

As stated earlier, a block-oriented methodology is used to model the Wissler simulated data for this study. The following section of this chapter will discuss the methodology used for modeling and also introduce previous work where this methodology was applied to the human thermoregulatory system.

2.4 Continuous-Time Hammerstein Modeling and H-Best

The dynamic modeling approach followed in this study is a continuous-time methodology developed from an exact solution to Hammerstein systems [21]. The Hammerstein system is a class of nonlinear dynamic processes, which combines a nonlinear static gain block with a linear dynamic block as shown in the Fig. 2.3. That is, the static gain block is nonlinear with respect to the time-dependent variables. Hence, the dynamic block is a linear differential equation with respect to the time-dependent variables.

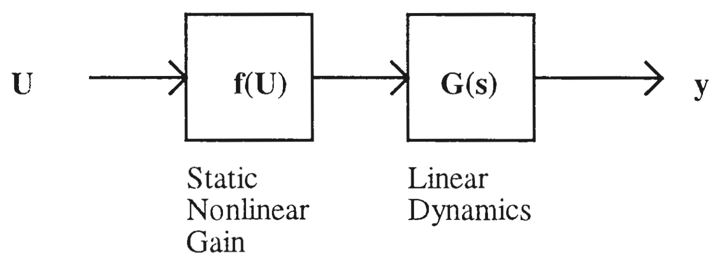

Figure 2.3: Schematic drawing of a general MIMO Hammerstein model as shown in [21]. The **U** represents a deviation vector of the inputs. First, the static nonlinear element, **f(U)**, scales the input vector **U**, and then **U** is passed through the linear dynamic transfer function **G(s)**, which produces the output vector **y**.

A number of articles in the literature explore the identification of nonlinear models using the Hammerstein structure. For example, nonparametric approaches to the Hammerstein identification has been proposed and developed by Greblicki [15] and Pawlak [22]. The Hammerstein approach has been used in many cases, most of which are simulations. For example, Eskinat e. al. [10] used the Hammerstein structure for modeling a simulated distillation column and an experimental heat exchanger. Currently, most Hammerstein model approaches that have been used are discrete-time in nature. However, there are some critical drawbacks to discrete-time models. Mainly there are important drawbacks when sampling is infrequent or non-constant. In addition, the modeling identification can be rather extensive due to the large amount of estimated parameters, depending on the sampling rate and number of input variables. There is also limitation in extrapolation when using discrete-time models. Greblicki [15] developed a continuous-time solution to the Hammerstein. However, it seems that our methodology is the first compact closed-form continuous-time exact solution to the Hammerstein system. Hence, the methodology that we propose consists of a continuous-time model and hence, it does not have the drawbacks that discrete-time models have.

The proposed approach is called **H**ammerstein **B**lock-oriented **E**xact **S**olution **T**echnique, **H-BEST** and was proposed by Rollins et al. [27]. The introduction of H-BEST involved a single-input, single-output (SISO) study of a continuous stirred tank reactor (CSTR) by Rollins et al. [27]. Further studies revealed H-BEST's ability to predict accurately for a variety of output sampling situations, including no sampling of the output by Bhandari et al. [3]. Rietz et al. [23] demonstrated the implementation of H-BEST's simple prediction algorithm into a real SISO continuous process connected to a distributed control system.

More recently, Rollins et al. [27] showed the ability of H-BEST to model complex dynamics (e.g. underdamped and inverse response) exceptionally well. Again, H-BEST performed well for cases of no output sampling, and variable input change rate. Rollins et al. [25] successfully applied the H-BEST algorithm to a multiple-input, multiple-output (MIMO) case of a household dryer. This proposed approach is the only block-oriented method that we have found to be able to address the interaction effects of input levels and to be able to take full advantage of statistical design of experiment.

H-BEST applications have not been limited to chemical process. Walker [32] successfully used H-BEST in SISO modeling of a surrogate human's (a mathematical human model, the Wissler model) thermoregulatory response to the change in ambient conditions. As stated earlier the H-BEST is an exact solution to the Hammerstein processes for step input changes. This discovery was quit recent and a mathematical proof of the solution is provided in [24]. However, the next section will briefly present the H-BEST closed-form exact solution to the Hammerstein.

2.4.1 The Exact Solution.

This section presents the general solution to the Hammerstein process for step input change as given in Rollins, et. al. [27]. This solution is restricted to step input changes and for other inputs cases, H-BEST's ability to predict depends on how well the input series can be approximated by piecewise step functions. The solution is based on the block structure in Fig. 2.3. For step changes in $\mathbf{U}(t)$ occurring at times $t = 0, t_1, t_2 \ldots$, as given in Eq. 2.10, the following closed-form exact solution to Hammerstein systems, the H-BEST algorithm, is given as showed in Eq. 2.11 below.

Step Input Changes:

$$\mathbf{U(t)} = \begin{cases} \mathbf{U(0)} & for\ 0 \le t < t_1 \\ \mathbf{U(t_1)} & for\ t_1 \le t < t_2 \\ . & \\ . & \\ . & \end{cases} \tag{2.10}$$

The H-BEST algorithm:

$$\begin{aligned} 0 \le t < t_1: &\quad y(t) = y(0) + f(\mathbf{U}(t_0); \boldsymbol{\beta}) \bullet g(t; \boldsymbol{\tau}) \\ t_1 \le t < t_2: &\quad y(t) = y(t_1) + [f(\mathbf{U}(t_1); \boldsymbol{\beta}) - y(t_1) + y(0)\,] \bullet g(t-t_1; \boldsymbol{\tau}) \\ t_2 \le t < t_3: &\quad y(t) = y(t_2) + [f(\mathbf{U}(t_2); \boldsymbol{\beta}) - y(t_2) + y(0)\,] \bullet g(t-t_2; \boldsymbol{\tau}) \end{aligned} \tag{2.11}$$

and so on...

where $y(t)$ is the output response at time t; $y(0)$ is the measured value of the output at the initial time zero; $\mathbf{U}(t)$ is the input vector that contains the deviation values of the process input variables at time t; $f(\mathbf{U}(t); \boldsymbol{\beta})$ is any nonlinear static gain function; $\boldsymbol{\beta}$ is the vector of the static gain function parameters; and $\boldsymbol{\tau}$ is the vector of the dynamic parameters. The dynamic function, $g(t; \boldsymbol{\tau})$, is described by Eq 2.12 below.

$$g(t; \boldsymbol{\tau}) = L^{-1}\left(G(s) \cdot \frac{1}{s} \right) \tag{2.12}$$

where L^{-1} is the inverse Laplace transform operator; and G(s) is a linear dynamic transfer function. Note that, as $t \to \infty$, the function of $g(t) \to 1$ and $y(t) \to y(0) + f(\mathbf{U}(t))$. Thus, the H-BEST algorithm provides proper limiting behavior. The algorithm can be modified to include dead time and measured response data (see Rollins et al [25]).

The methodology of identifying the H-BEST model is based on the knowledge gained from this exact solution. The methodology can be described in the following steps. The first steps to obtain the H-BEST model for the proposed approach is to use an appropriate statistical design of experiment for the chosen input variables over the input space. The second step is to run each experimental trial allowing the process to reach the new steady state and collect data over time for each run. The third step is to use the steady state data to model the nonlinear static gain function $f(\mathbf{U}(t); \boldsymbol{\beta})$ and estimate the static gain parameters. The fourth step is to use the transient data to determine the form of the dynamic function g(t; τ) and estimate the dynamic parameters. As stated earlier, H-BEST was applied to a single-input, single-output (SISO) case of modeling of the human thermoregulatory system. The following section will describe this study in further detail.

2.5 SISO H-BEST ALGORITHM APPLIED TO THE HUMAN THERMOREGULATION

As stated earlier, the H-BEST approach has not only been used on chemical processes but also been applied to biological systems. Walker [32] did a SISO H-BEST study of modeling the human thermoregulatory system by using the Wissler [36] model as the experimental subject. In this study the response of the skin temperature was dynamically modeled for step changes in the room temperatures from 10 to 90 °F. The initial values of the runs represents a man clothed in cotton shorts, weighing 182 lbs., with a mean skinfold thickness of 12 mm, and with a resting metabolic rate of 285.76 BTU/hr. The ambient conditions were set at 0.5 mph for the wind speed and the relative humidity is set at 30%. The steady state room temperature was set at 65 ° F, with changes made once the body had reached a steady state for that temperature. The H-BEST model was obtained by making step changes in the room temperature, and the skin temperature response provided data to obtain the static gain and dynamic function. The form of the linear transfer function for this study was a second order model with a single zero. The general form of the derived H-BEST algorithm is given by Eq. 2.13 below for

$t_{k-1} \leq t \leq t_k$:

$$\hat{T}_{Skin} = \hat{T}_{Skin,t_{k-1}} + \left(a + b\Delta T_{Room} + \hat{T}_{Skin,0} - \hat{T}_{Skin,t_{k-1}}\right) \times \left(1 + \frac{\tau_a - \tau_1}{\tau_1 - \tau_2} e^{-\frac{t-t_{k-1}}{\tau_1}} + \frac{\tau_a - \tau_2}{\tau_2 - \tau_1} e^{-\frac{t-t_{k-1}}{\tau_2}}\right) \tag{2.13}$$

The main goal of this study is to investigate H-BEST's ability to accurately predict dynamic response behavior for an arbitrary input sequence. The input sequence used for the study is shown in Figs. 2.4 and 2.5 is the plot of the actual and predicted skin temperatures. As shown, the fit is very good and Walker concluded that H-BEST showed much promise for modeling of the human thermoregulatory system.

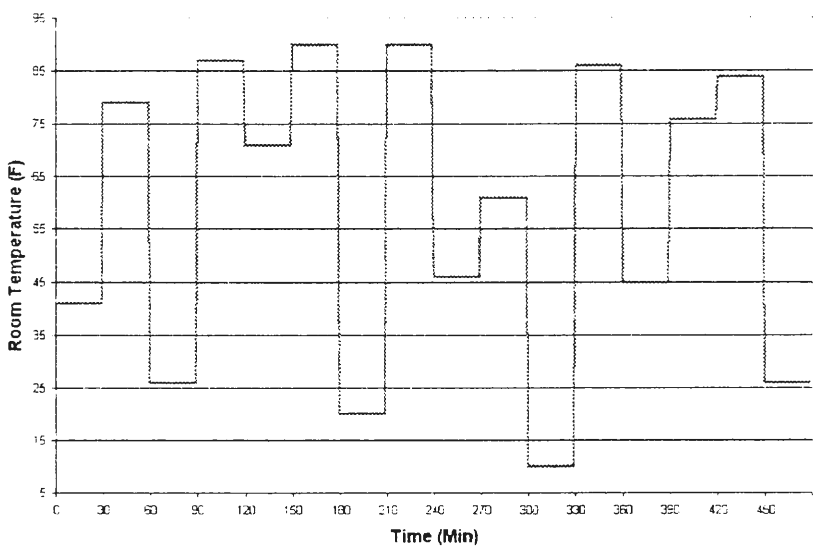

Figure 2.4: Sequence of the step changes in input, i.e. the room temperature.

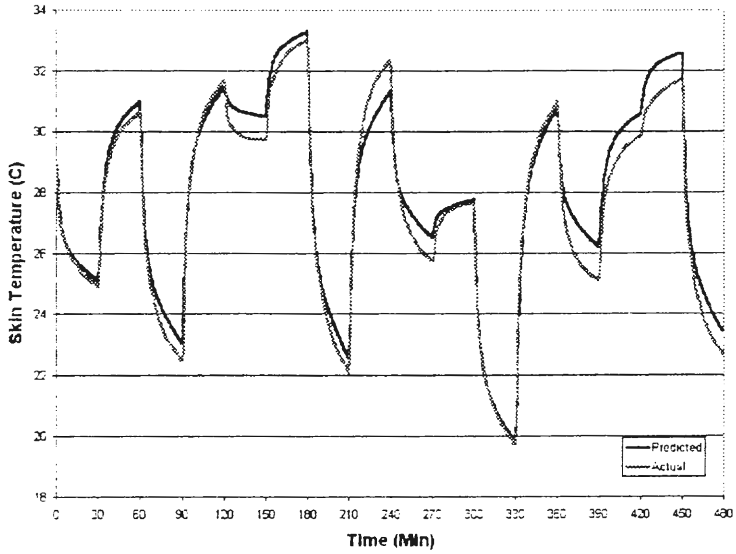

Figure 2.5: The values simulated by Wissler and the predicted values by H-BEST for skin temperature.

2.6 SUMMARY OF CHAPTER

The principle objective of this chapter is to describe methods of modeling the human thermoregulatory system. While different modeling techniques are mentioned in this chapter, the main focus is on the semi-theoretical model given by Wissler [36] that is used as the surrogate human for this study. The Wissler model is, in accordance with most thermoregulatory models, a computer program. The Wissler computer program with its associated files is also described in detail. In addition, the modeling approach used for this study, referred to as H-BEST is also described in detail. The last section of this chapter includes the first application of H-BEST to model the human thermoregulatory system. Walker [32] concluded that the approach has much promise as a method in this application.

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CHAPTER 3. EFFECTIVE MIMO MODELING OF THE HUMAN THERMOREGULATORY SYSTEM

A paper to be submitted to IEEE Transactions

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ABSTRACT

This study investigates the ability to efficiently and practically model the human thermoregulatory system (HTS) with a block-oriented approach for a multiple-input, multiple-output (MIMO) case. This approach is a new compact, continuous-time, closed form methodology developed that approximates processes with a Hammertein structure [7]. It is called the **H**ammerstein **B**lock-oriented **E**xact **S**olution **T**echnique (H-BEST). In this study H-BEST is used to develop highly accurate models of sweat rate and skin temperature for changes in environmental variables, by using the Wissler model (1964) as a surrogate human. The input variables for the study are the environmental temperature, the relative humidity, and the wind speed. A powerful characteristic to this methodology is its ability to make full use of Statistical Design of Experiments (SDOE) for optimal data collection with accurate parameter estimation. This work shows much promise in developing accurate dynamic closed-form models for a MIMO case of the HTS.

Key words: Effective modeling, Multiple-input multiple-output, Human Thermoregulatory System, Hammerstein process, Dynamic modeling

3.1. INTRODUCTION

Several recent developments, such as the tightening of industrial health and safety standards, stricter controls over the allowable use of human and animal subjects in experiments, and the continued expansion of military, industrial, and scientific efforts in hostile environments, suggest the need for improved models of physiological systems. Hence, the objective of this study is to develop an accurate predictive model for the HTS. As stated earlier, experiments on human subjects can be both costly and inhumane in some cases. Hence, the basic objective of this study is to develop predictive model of the HTS from a relatively small amount of experimental trials.

The need for improved knowledge of the human thermoregulation has led to the development of various approaches of thermoregulatory modeling. There are mainly two approaches to model the HTS. The first approach, which is classified as the analytical approach, and also referred to as the theoretical approach, relies on the fundamental laws of science. That is, both the model structure and its parameters are derived from theory. This approach is very rigorous and requires complete theoretical understanding of the response behavior. For this reason, this approach is rarely used for complex modeling problems. The second approach is the empirical approach, which strongly relies on data, and the model structure and its parameters are empirically derived. As stated earlier, the objective of the proposed method is to obtain closed-form continuous-time model of the HTS from a minimal amount of experimental data.

This work exploits a new solution developed for the modeling of engineering processes that can be described by the block-oriented Hammerstein system that combines nonlinear static gains with linear dynamic systems. This method was developed by Rollins et al. [13] and it is called the **H**ammerstein **B**lock-oriented **E**xact **S**olution **T**echnique, H-BEST. H-BEST is a compact, continuous-time, solution that gives optimal (i.e., the smallest possible number) parameterization and preserves the form of the static gain functions. Hence, H-BEST will be used to obtain highly accurate models of sweat rate and skin temperature for changes in environmental variables. That is, the approach that this study will take will be to develop a H-BEST model for the two responses, by using the Wissler (1964) computer program as a surrogate human. The input variables of this study are the environmental temperature, the wind speed, and the relative humidity.

This paper presents this study in the following outline. The next section presents the general H-BEST solution. Following this section, the proposed methodology to obtain the H-BEST model is presented for a MIMO case of modeling the HTS. This methodology involves the use of SDOE. By using SDOE the number of required runs can be reduced significantly, while maintaining an ability to estimate the model parameters. Finally, the results and conclusions are presented.

3.2 H-BEST

This section will describe a general exact solution to Hammerstein systems developed by Rollins et al. [13] for step input changes.. The Hammerstein system [7] combines a nonlinear static gain block with a linear dynamic block as shown in the Figure 3.1.

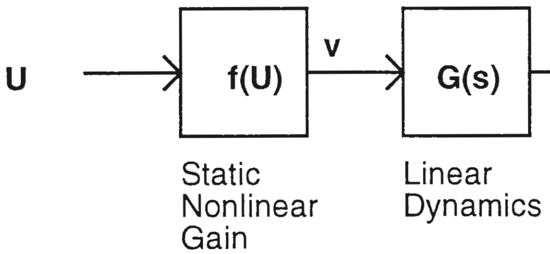

Figure 3.1: Schematic drawing of a general MIMO Hammerstein model as shown in [7]. The **U** represents the deviation vector of the inputs. The static nonlinear element, **f(U),** scales the input **U,** and then the inputs are transformed by a linear transfer function **G(s),** to produce the output vector **y**

A number of articles in the literature explore the identification of nonlinear models using the Hammerstein model, for example the work of Greblicki [5] and Pawlak [8]. The Hammerstein system is most commonly used for simulated processes. The work by Eskinat et. al. [4] uses the Hammerstein structure for modeling a simulated distillation column and an experimental heat exchanger. Historically, Hammerstein model approaches have been used in discrete-time applications, but there are some critical drawbacks to discrete-time modeling. These drawbacks are especially important when sampling is infrequent or non-constant. In addition, the modeling identification can be rather extensive due to the large amount of estimated parameters, depending on the sampling rate and number of input variables. There is also limitation in extrapolation when using discrete-time models.

Greblicki [5] developed a continuous-time solution to the Hammerstein. However, it seems like the H-BEST model is the first closed-form continuous time exact solution to the Hammerstein system. The general closed-form solution of a Hammerstein system for a series of step input changes at time $t = 0, t_1, t_2 \ldots,$ as given in Eq. 3.1, called the H-BEST algorithm is showed in Eq. 3.2 below.

Step Input Changes:

$$\mathbf{U(t)} = \begin{cases} \mathbf{U(0)} & \text{for } 0 \le t < t_1 \\ \mathbf{U(t_1)} & \text{for } t_1 \le t < t_2 \\ . & \\ . & \\ . & \end{cases} \tag{3.1}$$

H-BEST Algorithm:

$$0 \le t < t_1: \quad y(t) = y(0) + f(\mathbf{U}(t_0); \boldsymbol{\beta}) \bullet g(t; \boldsymbol{\tau}) \tag{3.2}$$

$$t_1 \le t < t_2: \quad y(t) = y(t_1) + [f(\mathbf{U}(t_1); \boldsymbol{\beta}) - y(t_1) + y(0)] \bullet g(t-t_1; \boldsymbol{\tau})$$

$$t_2 \le t < t_3: \quad y(t) = y(t_2) + [f(\mathbf{U}(t_2); \boldsymbol{\beta}) - y(t_2) + y(0)] \bullet g(t-t_2; \boldsymbol{\tau})$$

and so on...

where $y(t)$ is the output response at time t; $y(0)$ is the measured value of the output at the initial time zero; $\mathbf{U}(t)$ is an input vector that contains the deviation values of the process input variables at time t from time (t-1); $f(\mathbf{U}(t))$ is any nonlinear static gain function; $\boldsymbol{\beta}$ is the vector of the static gain function parameters; and $\boldsymbol{\tau}$ is the vector of the dynamic parameters. The dynamic function, $g(t; \boldsymbol{\tau})$, is described by Eq. 3.3 below.

$$g(t; \boldsymbol{\tau}) = L^{-1}\left(G(s) \cdot \frac{1}{s} \right) \tag{3.3}$$

where L^{-1} is the inverse Laplace transform operator; and G(s) is the linear dynamic transfer function of the process.

When this algorithm was first introduced in Rollins et. al. [13] it was not recognized as a exact solution to the Hammerstein process. This is a rather new discovery. The mathematical proof for the solution is given in [10]. The H-BEST method has proven itself to model well in many different circumstances. The works of Rollins et. al. [11, 12, 13], Reitz et. al. [9], Bhandari et. al. [1, 2], and Walker et.al. [15] demonstrate H-BEST's ability to predict well for noise, extrapolation, random changes of inputs, for a real process, for mathematically complicated processes, and biological systems for step input changes. The successful study for a SISO modeling of the human thermoregulation done by Walker [15] led to this study of a MIMO case of the HTS. The following section presents the experimental modeling approach taken in this study.

3.3. Experimental Modeling Approach

Currently, using a model of the HTS requires knowledge in both human thermoregulatory modeling and computer programming, since most models are computer-based simulations. There are a number of factors that needs to be considered before modeling human thermoregulation. For example, the possible factors considered when modeling the HTS are: body mass, air temperature, level of acclimatization, wind velocity, body height, relative humidity, age, cardio-vascular condition, gender, exercising level, and how rigorous the analysis need to be.

Likewise, there are several outputs that need to be taken into account. These outputs can be divided into two classifications: quantitative and qualitative outputs. The core temperature, skin temperature, water loss, and whether systems limitations were exceeded can be classified as quantitative outputs. Whereas, an estimation of how "comfortable" the given exercise (in the given environment) will be is considered to be qualitative outputs. In summary, the various steps to obtain the H-BEST model for the proposed approach are described below:

1. *Select the input variables and output variables*
2. *Define the input space*
3. *Use appropriate statistical design of experiment*
4. *Run each experimental trial allowing the process to reach a new steady state and collect data over time for each run.*
5. *Use the steady state data to model the nonlinear static gain function* $f(\mathbf{U}(t))$
6. *Use the transient data to determine the form and parameters of the dynamic function* $g(t)$

As given above, the first step is to select the input variables. This also involves identifying all the variables that affected the process and all the variables that can be manipulated and controlled. As stated earlier, there are a large number of input variables that can be considered for this approach. However, the input variables chosen in this study were the temperature of the environment (T), the relative humidity of the environment (H), and the wind speed of environmental air (W). Furthermore, the output variables, which are to be modeled, must also be decided. Thus, the output variables for the proposed model are the skin temperature and the sweat rate.

The next step is to determine the input space, also referred to as the operational region. Consequently, the upper and lower limits of the input variables were chosen from a realistic perspective so that they would cover as wide range as possible and have the potential to be of use in a real experiment. Recall that this study investigates the dynamic behavior of skin temperature and sweat rate. Hence, to be able to model the dynamic changes in the responses, the temperature of the environment should be higher than the body temperature. In these situations the loss of body heat then becomes very dependent on sweat evaporation. That is, for the sweat to evaporate the surrounding air must be relatively free of water for evaporation to occur. Thus, when the ambient humidity is high, the capacity of the environment to accept water is reduced. Hence, for this study the experimental region will consist of high temperatures, high relative humidity, and low wind speeds, which is an operational region for which the responses are highly affected by input changes. In addition, for each input variable, three different levels are chosen to model the curve linear effects on the ultimate response across the input space. Table 3.1 shows the three coded levels (-1, 0, 1) for each input variable.

Table 3.1: The three coded levels for each input variable.

Factor	**-1**	**0**	**1**
Temperature of Environment (T) [° F]	90	94	98
Wind speed (W) [mph]	1	3	5
Humidity (H) [%]	75	80	85

The third step is to find an appropriate SDOE to optimize the information content for estimating model parameters. The optimization is based on generating as few runs as possible, and still getting accurate estimates for the main effects and interactions of the inputs. In order to estimate the second order, quadratic, or nonlinear component of the relationship between output responses and the input variables, at least 3 levels for the respective factors need to be specified. A complete factorial design that models all possible interactions with three inputs at three levels requires $3^3 = 27$ trials. This number of trials is usually both costly and time consuming. Hence, we only considered experimental designs that fit both main effects and quadratic effects. The selected design was a Box-Behnken design (BBD) with 13 runs and no replication of center point. Keeping in mind that we are using computer-simulated data for this study, there is no need for replicated runs, since there is no deviation in simulated response when replicating a run. The choice of a BBD is based on the criteria that the number of experimental trials is minimized. A corresponding Central Composite Design would yield a total of 15 experimental trials, without replicating the center point. The BBD is an evenly spaced three-level design. The BBD is based on a balanced incomplete block design (BIBD) were each pair of the factors in the BIBD is treated as a 2^2 factorial with the rest of the factor levels set at 0. As stated in [6], one of the characteristics of the BBD is that it is a near-rotatable design. A rotatable design has a prediction variance that has the same value at any two locations that are the same distance from the design center. Another important characteristic of the BBD is that it is a spherical design. That is, for a design with 3 factors, all the "edge points" of the design is on a distance $\sqrt{2}$ from the design center. That is, the use of the BBD is limited to prediction in the "sphere" and should not be used for prediction of the responses at the corners of the experimental design. The 13 experimental trials for the BBD were generated by using the software package JMP version 4.0.4, SAS institute Inc. on a PC platform. Table 3.2 shows the levels of each input for the 13 experimental trials.

Table 3.2: The 13 experimental trials used in this study.

Run #	T (°F)	W (mph)	H (%)
1	94	1	85
2	94	3	80
3	98	3	85
4	94	1	75
5	98	3	75
6	90	3	75
7	90	1	80
8	98	5	80
9	90	5	80
10	94	5	75
11	98	1	80
12	94	5	85
13	90	3	85

The fourth step to obtain the H-BEST model is the simulation part of this study consists of executing the 13 experimental trials, and plotting the output responses. The initial condition set for this study is valid for a man in a sitting position wearing a cotton shirt and pants, with a weight of 182 lbs., skinfold thickness 12 mm., resting metabolic rate of 285.76 BTU/hr, in an environment with temperature of 80 °F, an air pressure of 14.969 psia (1 atm.), a relative humidity of 50%, and a wind speed of 3 mph.

The fifth step is to use the steady state data to find the nonlinear static gain function for each of the responses by using regression. Below is the ultimate gain function (Eqs. 3.4. and 3.5) for the two responses with significance declared at the 0.05 level.

Skin temperature nonlinear static gain function:

$$\hat{f}_{Tskin}(\Delta T, \Delta H, \Delta W; \hat{\beta}) = 0.81 + 0.29 * \Delta T + 0.013 * \Delta H - 0.15 * \Delta W \\ - 0.0056 * \Delta T^2 - 0.0011 * \Delta T * \Delta H + 0.0094 * \Delta T * \Delta W \tag{3.4}$$

Sweat rate nonlinear static gain funciton:

$$\hat{f}_{Sweat}(\Delta T, \Delta H, \Delta W; \hat{\beta}) = 4.83 - 0.54 * \Delta T - 0.13 * \Delta H - 0.091 * \Delta W \\ + 0.017 * \Delta T^2 + 0.011 * \Delta T * \Delta H \tag{3.5}$$

where the ΔT, ΔH, ΔW terms are input deviation variables from the initial conditions. The last step in model identification is to model the dynamics of the response. The dynamic model forms were selected by visually inspecting the output responses. For the skin temperature response a second order over damped with lead model form was selected and for the sweat rate a second order critically damped with lead and dead time model was selected. The dynamic parameters for the linear dynamic models are obtained by using nonlinear regression to fit the dynamic response for each run. The estimates of the dynamic parameters ($\hat{\tau}$'s) do not change significantly between the runs so the average values over the 13 runs are used in this study. Below are the dynamic functions (Eqs. 3.6 and 3.7) for the two responses:

Skin temperature dynamic function:

$$\hat{g}_{Tskin}(t; \hat{\tau}) = 1 + \frac{(\hat{\tau}_a - \hat{\tau}_1)}{(\hat{\tau}_1 - \hat{\tau}_2)} e^{-t/\hat{\tau}_1} + \frac{(\hat{\tau}_a - \hat{\tau}_2)}{(\hat{\tau}_2 - \hat{\tau}_1)} e^{-t/\hat{\tau}_2} \tag{3.6}$$

$$\hat{\tau}_1 = 1.75$$
$$\hat{\tau}_2 = 40.69$$
$$\hat{\tau}_a = 14.27$$

Sweat rate dynamic funciton:

$$\hat{g}_{Sweat}(t;\hat{\tau}) = \left(1 + \left(\left(\frac{(\hat{\tau}_a - \hat{\tau})}{\hat{\tau}^2}\right)(t-\hat{\theta}) - 1\right)e^{-(t-\hat{\theta})/\hat{\tau}}\right) \tag{3.7}$$

$$\hat{\theta} = 376.06 - 33.83 * \Delta T + 16.31 * \Delta W$$
$$+ 0.82 * \Delta T^2 - 0.94 * \Delta T * \Delta W$$
$$\hat{\tau} = 50.94$$
$$\hat{\tau}_a = 32.81$$

where the $\hat{\tau}$'s are the estimates of the dynamic parameters found by using nonlinear regression; and $\hat{\theta}$ is the dead time parameter, which is estimated by using linear regression. Since the dead time varies over the input space, the prediction of the dead time is modeled as a function of the input variables. The estimates for the dead time equation were all found to be significant at the 0.05 level. Figs. 3.2 and 3.3 represent the generated skin temperature and sweat rate data for Run 3 with the fitted dynamic model, respectively.

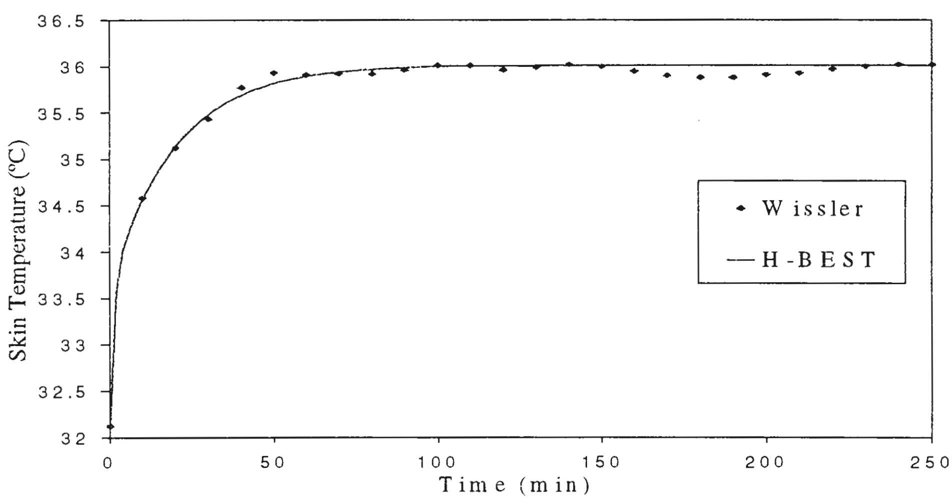

Figure 3.2: The dynamic response of the skin temperature values generated by the Wissler model and the fitted H-BEST model of the skin temperature for Run 3 in Table 3.2.

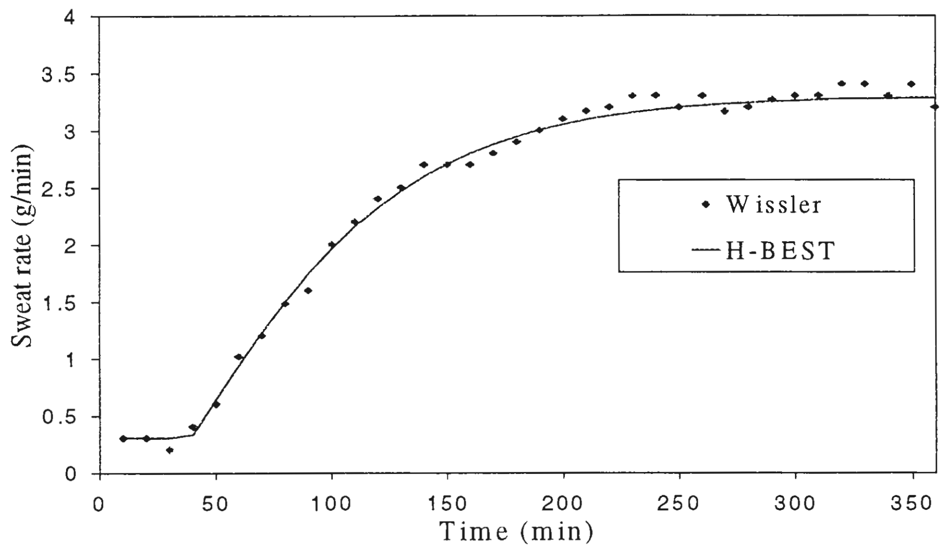

Figure 3.3: The dynamic response of the sweat rate values generated by the Wissler model and the fitted H-BEST model of the sweat rate for Run 3 in Table 3.2.

3.4 RESULTS

The main objective of this work is to investigate the ability of H-BEST to model a MIMO case of the HTS. Thus, this section presents the simulation study to evaluate the H-BEST model's ability to accurately and practically model the skin temperature and sweat rate response for changes in the input variables. As stated earlier, the input variables are the environmental temperature (T), humidity (H), and wind speed (W). To optimize the experiments, which means executing as few runs as possible but still getting a good estimate for the main effects and interactions of the inputs, SDOE is used for model identification. Accordingly, for the proposed approach a BBD with 13 experimental trials is used.

The ability of H-BEST to model the HTS was investigated for a randomly generated input sequence, also called test sequence, as showed in Fig. 3.4. The Fortran computer code for the test sequence is given in Appendix A. That is, the input variables were changed randomly with step input changes within the input space of the study. The simulated data by the Wissler model and the output responses predicted by H-BEST are given in Figs. 3.5 and 3.6. The predictions from H-BEST are seen to agree well with the simulated data. That is, there is not a significant deviation between the simulated data and the predicted data.

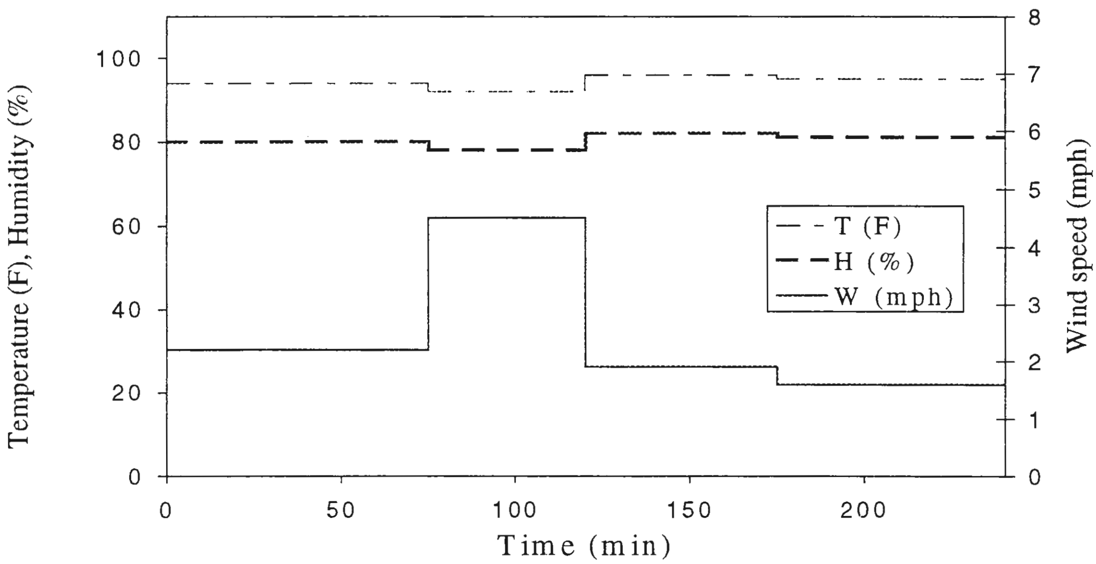

Figure 3.4: The input sequence used for evaluating the H-BEST model.

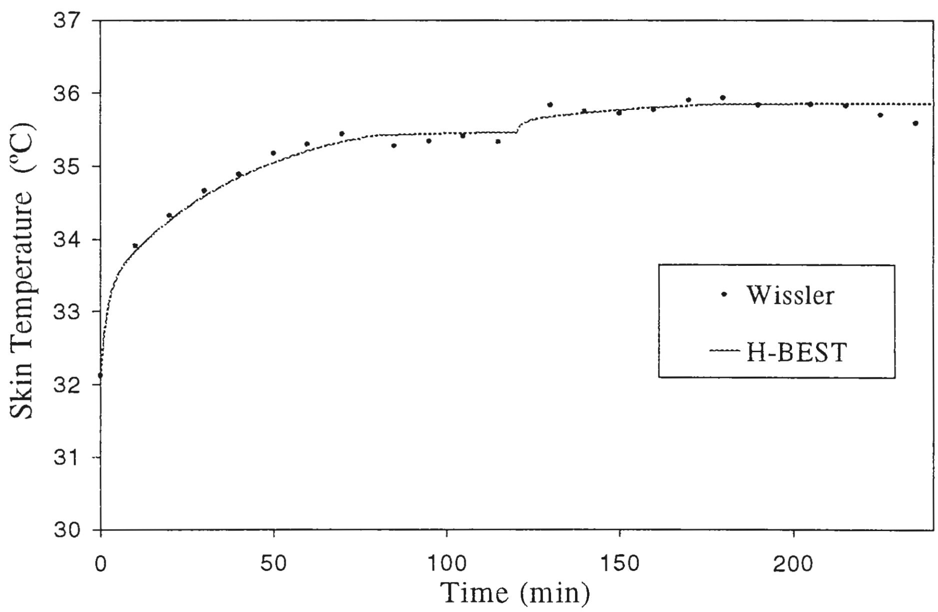

Figure 3.5: The Wissler simulated skin temperature values and the predicted H-BEST model for the input sequence shown in Figure 3.4.

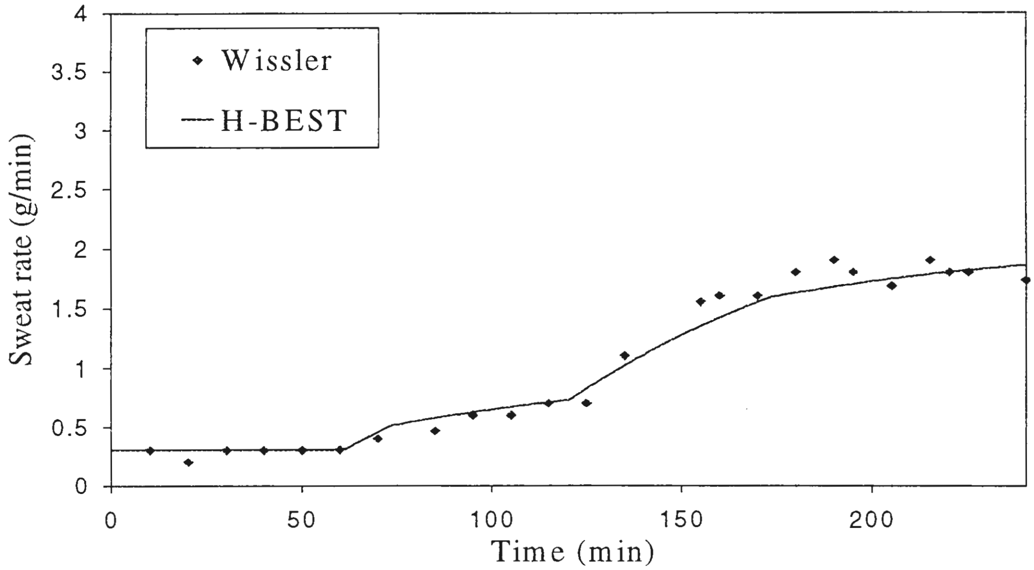

Figure 3.6: The Wissler simulated sweat rate values and the predicted H-BEST model for the input sequence shown in Figure 3.4.

For the skin temperature response the H-BEST prediction closely follows the simulated data for throughout the input sequence. That is, there are no significant deviation between the simulated data and the fitted dynamic data. The same conclusion can be made for the sweat rate response. The generated sweat rate data has more noise in it compared to the skin temperature data, but it seems like H-BEST captures the sweat rate response behavior very well. Thus, H-BEST shows much promise for accurately predict responses of the HTS.

3.5 Conclusions

The potential of using H-BEST for modeling the HTS for a three-inputs, two- outputs case by using the Wissler [17] model as a surrogate human has been investigated in this paper. The study showed that H-BEST can accurately predict the responses of skin temperature and sweat rate for changes in the environment. Since the H-BEST approach is an exact solution to Hammerstein systems, the H-BEST shows to be very accurate in prediction when the process is Hammerstein or approximately Hammerstein in nature.

There are a few things that need to be taken into consideration for this approach. First, the lack of steady state value for the output responses is a characteristic of the simulator used to generate the data and not of the actual human thermoregulatory process. It is likely that the H-BEST method would predict better for actual experimental data. Secondly, although the model does a reasonably good job of describing individual response over a broad range of conditions, one should extrapolate outside these conditions with care.

Future research would consist of developing dynamic models for the HTS from human subjects. There are two issues that cause concern when planning to model the HTS using humans as experimental subjects. These are the number of experimental trials and the length of time for each experiment. The H-BEST solution will help to overcome these two major challenges in modeling the HTS. First, the H-BEST solution to can be used to significantly reduce the number of experimental trials per subject by finding an optimal experimental design. Secondly, the H-BEST solution can be used in optimal experimental design to significantly reduce the required time a subject needs to be in the environmental chamber for data collection. Solving these issues will give a practical procedure for modeling humans as subjects. Future research would of course also consist of exploring other input regions and other response variables than what was used for this study. In addition, in this study only step input changes were used. However, the changes in environmental conditions are rarely step changes in nature, but rather ramp input changes. Thus, potential future research work would also consist of developing a procedure for modeling the HTS for a ramp input change.

NOMENCLATURE

T = Temperature of the environment
H = Relative humidity of the environment
W = Wind speed of ambient air
t = time
U = vector of input variables
y = vector of output variables

Greek Letters

β = Vector of parameter in the static gain function of the outputs
τ = Vector of parameter in the dynamic function of the outputs
θ = Dead time for the dynamic function of the sweat rate response

Subscripts

Tskin = Skin Temperature
Sweat = Sweat rate

Superscripts

^ = Estimate

Abbreviation

BBD	=	Box-Behnken Design
BIBD	=	Balanced Incomplete Block Design
H-BEST	=	Hammerstein Block-oriented Exact Solution Technique
HTS	=	Human Thermoregulatory System
MIMO	=	Multiple input multiple output
SISO	=	Single input single output
SODE	=	Statistical Design of Experiments

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CHAPTER 4. ACCURATE PREDICTIVE MODELING WITH OPTIMAL EXPERIMENTAL DESIGN OF THE HUMAN THERMOREGULATORY SYSTEM

A paper to be submitted to Annals of Biomedical Engineering Journal

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ABSTRACT

The need for understanding the human thermoregulatory system has increased and so has the importance of developing accurate dynamic models for the thermoregulatory system. Historically, there have been mainly two modeling approaches for the human thermoregulatory system --theoretical and empirical. However, there are limitations to both of these approaches. The complexity and the lack of knowledge of the physiological behavior of the human body limit the theoretical approach. The empirical approach is unsuitable for practical use, due to the large amount of data requirements. This study is unique in the sense that it utilizes a new methodology that can develop accurate compact closed-from predictive models from a small amount of data.

This work exploit a new predictive modeling methodology developed for engineering processes that approximate the block-oriented Hammerstein structure. It is called the **H**ammerstein **B**lock-oriented **E**xact **S**olution **T**echnique (H-BEST) and is based on compact,

continuous-time, closed form solution that gives optimal (i.e., the smallest possible number) parameterization and preserves the form of the static gain functions.

The approach that this study will take is to use the H-BEST for modeling of the skin temperature and sweat rate, by using the Wissler (1964) computer program as a surrogate human from an optimal (i.e. minimal) amount of experimental trials. Hence, a practical procedure is developed to accurately predict the human thermoregulatory system from human subjects.

Keywords: Predictive Dynamic Thermoregulation Modeling, Design of Experiments, D-Optimality.

4.1. Introduction

In recent years humans have started to work and explore in more environmentally hostile and extreme conditions. Therefore, the need for understanding the human thermoregulatory system (HTS) has increased and so has the importance of developing dynamic models for the HTS. By modeling and simulating the HTS, it has become possible to study and predict the effect of these extreme environments on the human body. These extreme environments can have serious effects on our health. Especially, heat-related health problems such as heat cramps, heat exhaustion and heat-stroke have the highest probability of occurring in bright sunshine, high temperature and high humidity conditions. Thus, the main objective of this study is to accurately predict the skin temperature and sweat rate in these extreme conditions of high humidity and high temperatures using data from an optimal design. The optimization is based on minimizing the number of experimental trials and the time length for each experiment.

In literature, there are mainly two approaches to modeling the human thermoregulatory system. The first approach, which is classified as the analytical approach, and also referred to as the theoretical approach, completely relies on the fundamental laws of science. That is, both the model structure and its parameters are derived from theory. This approach is very rigorous and requires complete theoretical understanding of the process behavior, which is often not available. For this reason, this approach is rarely used for complex modeling problems such as modeling of the HTS. On the other hand, the empirical approach is unsuitable for practical use, due to the large amount of data required to empirically derive the models. This is especially true for situations when using humans as the experimental subject can be both costly and inhumane. Thus, the need to develop an accurate predictive model of the HTS from a small amount of data is of significant importance.

This work exploits a new methodology developed for the modeling of engineering processes that can be described by the block-oriented Hammerstein system that combines nonlinear static gains with linear dynamics. This method was developed by Rollins et al. [15] and it is called the **H**ammerstein **B**lock-oriented **E**xact **S**olution **T**echnique, or H-BEST. The approach that this study takes is to obtain predictive models based on H-BEST for the two output responses, skin temperature and sweat rate. The data used in model identification is generated by using the Wissler (1964) computer program acting as a surrogate human. Using models from H-BEST will help in addressing two major challenges faced when modeling the HTS. First, the H-BEST solution for the output responses will be used to significantly reduce the number of experimental trials per subject. Secondly, the H-BEST models will be used in optimal experimental design to significantly reduce the required time a subject needs to be in the environmental chamber for data collection. Thus, one of the main objectives of this study is to develop an efficient and practical procedure to model the skin temperature and sweat rate for different environments, when using humans as experimental subjects. The proposed study is unique in the sense that a closed-form continuous-time model for the HTS is developed from a minimal amount of experimental data.

This paper presents the proposed study in the following outline. The next section presents a closed-form exact solution to the Hammerstein process for a step input change. Following this section, is a description of the experimental approach involving identification of H-BEST, an optimization of numbers of experimental trials, and an optimization of experimental times. Finally, the results and conclusion are presented.

4.2. Exact solution to a Hammerstein system

As stated earlier, the dynamic modeling approach used for this study based on a compact closed-form continuous-time exact solution to the Hammerstein system. The Hammerstein system combines a nonlinear static gain block with a linear dynamic block as shown in the Fig. 4.1. Hence, for this study the assumption is made that HTS can be described by a Hammerstein process [9], and our exact solution to a Hammerstein process can be used to model the responses in this study. Thus, this section describes the general exact solution to Hammerstein systems developed by Rollins et. al. [15] for step input changes.

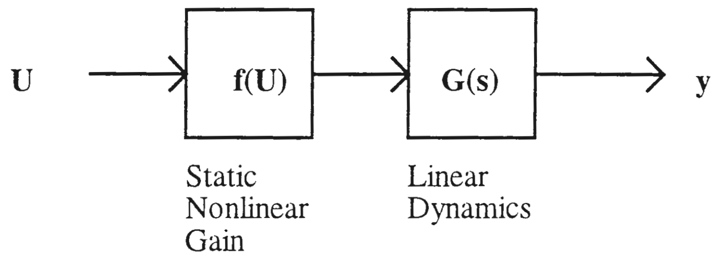

Figure 4.1: Schematic drawing of a general MIMO Hammerstein model as shown in [9]. The **U** represents a deviation vector of the inputs. First, the static nonlinear element, **f(U)**, scales the input vector **U**, and then **f(U)** is passed through the linear dynamic transfer function **G(s)**, which produces the output vector **y**.

A number of papers in the literature explore the identification of nonlinear models using the Hammerstein model, for example the work of Greblicki [7] and Pawlak [10]. The Hammerstein system is commonly used for simulated processes, as in the work by Eskinat e. al. [6], which used the Hammerstein structure for modeling a simulated distillation column and an experimental heat exchanger. Most commonly, Hammerstein model approaches have been used in discrete-time, but there are some critical drawbacks to discrete-time models. These drawbacks become especially important when sampling is infrequent or non-constant. In addition, the identification task can be rather extensive due to the large number of estimated parameters, depending on the sampling rate and number of input variables. There is also the limitation of extrapolation when using discrete-time models. The H-BEST closed-form solution to a Hammerstein system for a series of step input changes at time $t = 0, t_1, t_2 \ldots$, as given in Eq. 4.1, is given in Eq. 4.2 below:

$$\mathbf{U(t)} = \begin{cases} \mathbf{U(0)} & for\ 0 \le t < t_1 \\ \mathbf{U(t_1)} & for\ t_1 \le t < t_2 \\ . & \\ . & \\ . & \end{cases} \tag{4.1}$$

H-BEST Algorithm:

$0 \le t < t_1$: $\quad y(t) = y(0) + f(\mathbf{U}(t_0); \boldsymbol{\beta}) \bullet g(t; \boldsymbol{\tau})$ (4.2)

$t_1 \le t < t_2$: $\quad y(t) = y(t_1) + [f(\mathbf{U}(t_1); \boldsymbol{\beta}) - y(t_1) + y(0)] \bullet g(t-t_1; \boldsymbol{\tau})$

$t_2 \le t < t_3$: $\quad y(t) = y(t_2) + [f(\mathbf{U}(t_2); \boldsymbol{\beta}) - y(t_2) + y(0)] \bullet g(t-t_2; \boldsymbol{\tau})$

and so on....

where $y(t)$ is the output response at time t; $y(0)$ is the measured value of the output at the initial time zero; $\mathbf{U}(t)$ is an input vector that contains the deviation values of the process input variables at time t; $f(\mathbf{U}(t))$ is any nonlinear static gain function; $\boldsymbol{\beta}$ is the vector with parameters in the static gain function; and $\boldsymbol{\tau}$ is the vector of the dynamic parameters. The dynamic function, $g(t; \boldsymbol{\tau})$, is described by Eq. 4.3 below.

$$g(t;\boldsymbol{\tau}) = L^{-1}\left(G(s)\cdot\frac{1}{s}\right) \qquad (4.3)$$

Where L^{-1} is the inverse Laplace transform operator; and G(s) is the linear dynamic transfer function of the process, shown in Eg. 4.2.

When this algorithm was first introduced by Rollins et al. [15] it was not recognized as a exact solution to the Hammerstein process. This is a rather new discovery. The mathematical proof for the solution is given in [12]. The H-BEST method has proven itself to model well in many different circumstances. The works of Rollins et al. [12, 13, 14, 15], Reitz et al. [11], Bhandari et al. [3, 4], and Walker et al. [17] demonstrate H-BEST's ability to predict well for noise, extrapolation, random changes of inputs, for a real process, for mathematically complicated processes, and biological systems. The successful single-input, single-output (SISO) modeling of the human thermoregulation done by Walker [17] led to this proposed study of a multiple-input, multiple-output (MIMO) case of the HTS. The methodology used in this study is described in detail in the following section.

4.3. EXPERIMENTAL MODELING APPROACH

The main objective of this study is to find a practical and optimal experimental design for modeling the skin temperature and sweat rate for changes in the environment by using the Wissler program [19] as a surrogate human. The input variables chosen for the study are the ambient temperature (T), relative humidity (H), and wind speed (W).
Specifically, the approach taken in this study is to first use Statistical Design of Experiment (SDOE) to identify the H-BEST models from a small amount of experimental trials. After that the H-BEST algorithm is used to further reduce the number of experimental trials, while maintaining high information content for estimating the parameters. Thirdly, the H-BEST algorithm is used to minimize the length of each experiment trial, again without critical information in estimating the parameters. The following subsections of this chapter will discuss in detail the methodology used in this study.

4.3.1 H-BEST Algorithm

The methodology for developing an H-BEST model is described in the following steps. The first step is to use an appropriate SDOE for the chosen input variables over the input space. By using SDOE, the model parameters can be estimated from a conservative number of experimental trials. The second step is to run each experimental trial allowing the process to reach new steady state and collect data over time for each run. The third step is to use the steady state data to model the nonlinear static gain function $f(\mathbf{U}(t); \boldsymbol{\beta})$. The fourth and last step is to use the transient data to determine the form of the dynamic function g(t; τ) and estimate the dynamic parameters.

The H-BEST model in this study is obtained by using a Box-Behnken experimental design (BBD) of 13 runs. There is no need to replicate the center point of the design, since the experimental data comes from a computer simulation without random deviation added. Hence, the simulation part of this study consists of executing the 13 experimental trials as found in Table 4.1, and plotting the output responses. The initial conditions simulates a man in a sitting position wearing a cotton shirt and pants, with a weight of 182 lbs., skinfold thickness 12 mm., resting metabolic rate of 285.76 BTU/hr, and in an environment with temperature of 80 °F, an air pressure of 14.969 psia, a relative humidity of 50%, and a wind speed of 3 mph.

Table 4.1: The 13 experimental trials from the BBD.

Run #	**T (°F)**	**W (mph)**	**H (%)**
1	94	1	85
2	94	3	80
3	98	3	85
4	94	1	75
5	98	3	75
6	90	3	75
7	90	1	80
8	98	5	80
9	90	5	80
10	94	5	75
11	98	1	80
12	94	5	85
13	90	3	85

As stated earlier, the steady state data from the 13 experimental trials in Table 4.1 is used to derive the nonlinear static gain function, f(**U**(t), **β**) by regression for both the responses. The dynamic transfer function model forms for the two responses were selected by visually inspecting the output responses. For the skin temperature response, a second order overdamped with lead model was selected. For the sweat rate, a second order critically damped with lead and dead time model was selected. Estimates for the dynamic parameters in the linear dynamic models of the responses are obtained by using nonlinear regression to fit the dynamic response for each experimental trial. The dynamic parameters do not change significantly between the runs so the average values over the 13 runs are used in this study. The H-BEST static gain and dynamic models for the skin temperature and sweat rate are given in Eqs. 4.4 - 4.5 and Eqs. 4.6 - 4.7, respectively.

<u>Skin temperature static gain and dynamic functions:</u>

$$\begin{aligned}\widehat{f}_{Tskin}(\Delta T,\Delta H,\Delta W;\widehat{\beta}) = {} & 0.81+0.29*\Delta T+0.013*\Delta H-0.15*\Delta W \\ & -0.0056*\Delta T^2-0.0011*\Delta T*\Delta H+0.0094*\Delta T*\Delta W\end{aligned} \tag{4.4}$$

$$\begin{aligned}&\widehat{g}_{Tskin}(t;\widehat{\boldsymbol{\tau}}) = 1+\frac{(\widehat{\tau}_a-\widehat{\tau}_1)}{(\widehat{\tau}_1-\widehat{\tau}_2)}e^{-t/\widehat{\tau}_1}+\frac{(\widehat{\tau}_a-\widehat{\tau}_2)}{(\widehat{\tau}_2-\widehat{\tau}_1)}e^{-t/\widehat{\tau}_2} \\ &\widehat{\tau}_1 = 1.75 \\ &\widehat{\tau}_2 = 40.69 \\ &\widehat{\tau}_a = 14.27\end{aligned} \tag{4.5}$$

<u>Sweat rate static gain and dynamic functions:</u>

$$\begin{aligned}\widehat{f}_{Sweat}(\Delta T,\Delta H,\Delta W;\widehat{\beta}) = {} & 4.8-0.54*\Delta T-0.13*\Delta H-0.091*\Delta W \\ & +0.017*\Delta T^2+0.011*\Delta T*\Delta H\end{aligned} \tag{4.6}$$

$$g_{Sweat}(t;\hat{\tau}) = \left(1+\left(\left(\frac{(\hat{\tau}_a-\hat{\tau})}{\hat{\tau}^2}\right)(t-\hat{\theta})-1\right)e^{-(t-\hat{\theta})/\hat{\tau}}\right) \tag{4.7}$$

$$\hat{\theta} = 376.06 - 33.83 * \Delta T + 16.31 * \Delta W$$
$$+ 0.82 * \Delta T^2 - 0.94 * \Delta T * \Delta W$$
$$\hat{\tau} = 50.94$$
$$\hat{\tau}_a = 32.81$$

where the terms $\Delta T, \Delta \mathrm{H}, \Delta \mathrm{W}$ are the deviation variables from the initial input condition; and $\hat{\theta}$ is the dead time parameter, which is estimated by using linear regression, since the dead time varies over the input space. The estimates for the parameters in the steady state gain and the dynamic model are all significant at the 0.05 level.

Figs. 4.2 and 4.3 represent the Wissler simulated values and the H-BEST fit for the skin temperature and sweat rate data for Run 3, respectively.

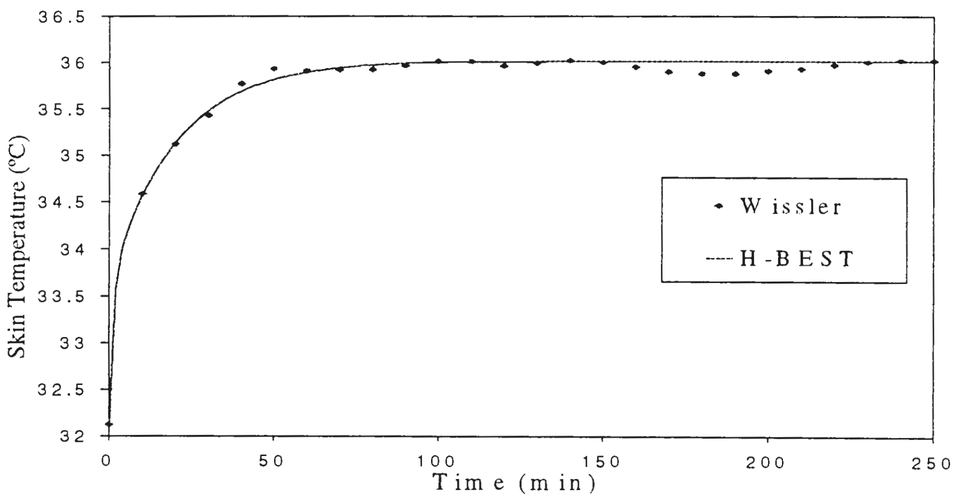

Figure 4.2: The dynamic response of the Wissler simulated skin temperature values and the H-BEST fitted skin temperature values for Run 3 in Table 4.1.

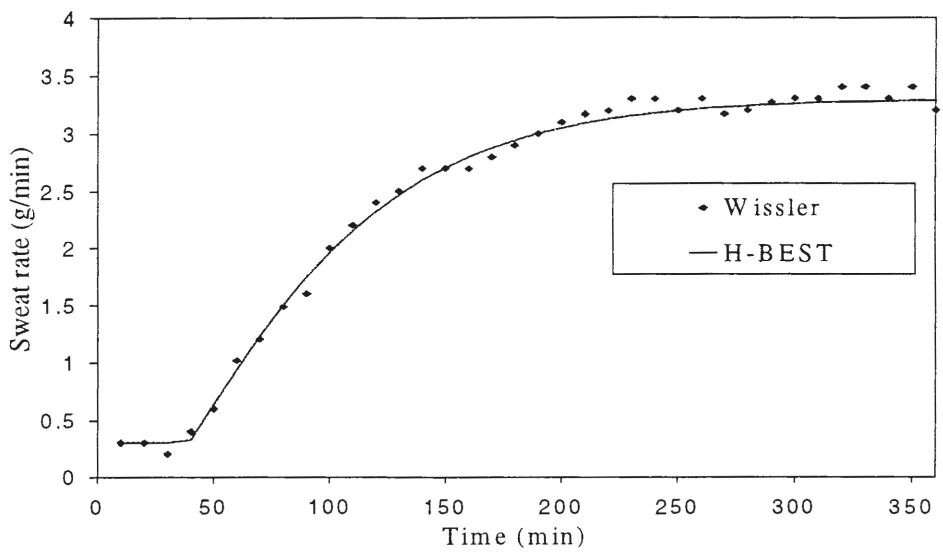

Figure 4.3: The dynamic response of the Wissler simulated sweat rate values and the H-BEST fitted sweat rate values for Run 3 in Table 4.1.

The next step was to use these fitted models to minimize the number of experimental trials. The approach taken for this optimization of the number of experimental trials is described in the following subsection.

4.3.2. OPTIMIZING THE NUMBER OF EXPERIMENTAL TRIALS

One of the main objectives of this study is to minimize the number of experimental trials needed to develop the H-BEST model without losing critical information for accurately estimating the parameters. When minimizing the number of trials, the number of parameters to be estimated needs to be taken into consideration. There are seven estimated parameters in the static gain equation, and three (τ_1, τ_2, and τ_a) estimated parameters in the dynamic equation for the skin temperature H-BEST model, as seen in Eqs. 4.4 - 4.5. There are six estimated parameters in the static gain equation, and three (τ, θ, and τ_a) estimated parameters in the dynamic equation for the sweat rate H-BEST model, as stated in Eqs. 4.6 - 4.7. Therefore, at least seven runs are needed for estimating the parameters in the H-BEST model.

The optimal design in this study is based on the D-optimality criterion, which seeks to find the design that minimizes the volume of the confidence region of the parameter estimates. That is, the size of the volume of the confidence region reflects how well the set of parameters is estimated. For statistically linear models, the square of volume of this confidence region is inversely proportional to the determinant of the $\mathbf{X}^T\mathbf{X}$, where $\mathbf{X}$ is the model input matrix. Hence, a D-optimal design (DOD) is one in which the $|\mathbf{X}^T\mathbf{X}|$ is maximized. Thus, this criterion is also referred to as the determinant criterion in literature. From a geometrical point of view, the D-optimal criterion implies a design in which the columns of $\mathbf{X}$ each have a vector that is as long as possible with orthogonal column vectors. Thus, the DOD will be spread out as much as possible over the input space and the parameter estimates will not be correlated.

The D-optimal criterion was applied to nonlinear functions as early as 1959 by Box and Lucas [1], where in place of the $\mathbf{X}$ matrix, the derivative matrix $\mathbf{V}^0$ evaluated at some initial parameter estimated $\boldsymbol{\theta}^0$ was used. As stated in Bates and Watts [2], for nonlinear models, the D-optimal criterion is the design that maximizes $\left|\mathbf{V}^{0\mathbf{T}}\mathbf{V}^0\right|$. Thus, the derivatives of the response are taken for each run with respect to the parameters in the model. Hence, if the experiemental function is linear in the parameters, then $\mathbf{V}^{0\mathrm{T}}\ \mathbf{V}^0$ is equal to $\mathbf{X}^\mathbf{T}\mathbf{X}$.

There are many statistical software packages that can find a DOD for a linear expectation function. However, for nonlinear expectation functions there does not appear to be a software package that can generate a DOD. Hence, finding the DOD for this study will be problematic, since the H-BEST model used in this study is a nonlinear function in the parameters. However, this problem was solved by assumptions in our methodology. As stated earlier, there are more static gain function parameters to be estimated than dynamic parameters for both of the two responses. Thus, we choose to use a saturated DOD based on the static gain equation for the two responses. That is, we would attempt to estimate the static gain parameters, $\boldsymbol{\beta}$ in the H-BEST model, with as few experimental trials as possible. Since, for this approach we are using the D-optimal criterion on a function that is linear in the parameters, we can use a commercially available software package to generate the DOD. However, the dynamic parameters will not be D-optimal, but since they are considerably fewer in number than the static gain parameters, we sought to obtain accurate estimates for them as well.

The required sample size for a saturated design for the skin temperature response is seven trials and for the sweat rate six trials. The DOD for the two responses were generated separately by the SAS version 8.02, SAS institute inc. software package. The computer code with the results for this simulation is found in Appendix B. The SAS software package finds a design for which the $|\mathbf{X}^{\mathrm{T}}\mathbf{X}|$ is maximized out of a list of candidate trials. For this study the list of candidate trials was comprised from a full 3-level factorial design with $3^3 = 27$ runs. The DOD for the skin temperature is given in Table 4.2 and the saturated DOD for the sweat rate is given in Table 4.3. The same designs were generated when executing the computer code five times in a row for different guesses of initial designs, which indicates that we can be confident in finding optimal designs.

Table 4.2: The saturated D-optimal design for the skin temperature

T (°F)	H (%)	W (mph)
90	75	3
90	85	1
90	85	5
94	85	5
98	75	3
98	85	1
98	85	5

Table 4.3: The saturated D-optimal design for the sweat rate

T (°F)	H (%)	W (mph)
90	75	5
90	85	1
94	75	1
94	85	5
98	75	5
98	85	1

From the SAS output, the determinant of information matrix, i.e., $\left|\mathbf{X}^T\mathbf{X}\right|$, is $e^{9.7041}$ for the skin temperature response and $e^{8.3178}$ for the sweat rate response. Some of the experimental trials in the two tables above are identical. However, we would still end up with a design with a number of runs close to 13 (7 (trials for skin temperature) + 6 (trials for sweat rate) - 3 (trials in common) = 10) when using the two designs separately to develop the H-BEST models. Note that the static gain models for the two outputs (Eqs. 4.4 and 4.6) differ only by the $\Delta T \Delta W$ interaction term, which is not significant in the sweat rate response as given in Eq. 4.6. This similarity in the models suggests that we could use the design that optimizes the skin temperature for both responses after evaluating how the information to get parameters for sweat rate is impacted. That is, check that there is not a significant loss of information in parameter estimation when developing the H-BEST model for the sweat rate response using the design in Table 4.2 instead of the design from Table 4.3. A measure of the fraction of information that is lost can be calculated using Eq. 4.8 below.

$$\eta_D^{*} = \left(\frac{\left|\mathbf{X}^{\mathbf{T}}\mathbf{X}\right|_{D1}}{\left|\mathbf{X}^{\mathbf{T}}\mathbf{X}\right|_{D2}} \right)^{1/p} \tag{4.8}$$

where p = 6 is the number of parameters in the static gain for sweat rate model. *D1* is the design in Table 4.2 and *D2* is the design in Table 4.3. The $\left|\mathbf{X}^{\mathbf{T}}\mathbf{X}\right|_{D1}$ is found manually by creating the model matrix, **X**, for the seven runs in Table 4.2 based on the static gain function of the sweat rate. The $\left|\mathbf{X}^{\mathbf{T}}\mathbf{X}\right|_{D2}$ is the value calculated by SAS. This is a modification of the D-efficiency as stated in Myers et. al [8]. In this modified version of efficiency the number of experimental trials in each design is not taken into account. Recall that the objective here is to use the seven runs given by the design in Table 4.2 without losing significant information in estimating the parameters for the static gain of the H-BEST sweat rate prediction. Thus, $\eta_D{*}$ from Eq. 4.8 provides a quantitative measure of the information content without taking the design size in consideration. The S-plus version 6.0, Lucent Technologies inc., software package was used to find these determinants. The computer code with the results can be found in Appendix C. The value of $\eta_D{*}$ is almost 1 (= 0.9999944). Therefore, there is practically no loss of information. Hence, the design from Table 4.2 appears to be a good choice to model both the skin temperature and sweat rate.

The H-BEST models were re-evaluated by running the seven experimental trials from the DOD in Table 4.2, and the dynamic and static parameters were re-estimated using the same procedure as before. Recall that the linear dynamic transfer function used for skin temperature response is a second order overdamped with lead model, and the dynamic transfer function for the sweat rate is a second order critically damped with lead and dead time model. The new H-BEST models developed from for the skin temperature and sweat rate are given in Eqs. 4.9 - 4.10 and Eqs. 4.11 - 4.12, respectively.

Skin temperature static gain and dynamic functions:

$$\hat{f}_{Tskin}(\Delta T, \Delta H, \Delta W; \hat{\beta}) = 1.16 + 0.27 * \Delta T - 0.0078 * \Delta H - 0.096 * \Delta W \\ - 0.0076 * \Delta T^2 + 0.0036 * \Delta T * \Delta W + 0.00096 * \Delta T * \Delta H \quad (4.9)$$

$$\hat{g}_{Tskin}(t; \hat{\tau}) = 1 + \frac{(\hat{\tau}_a - \hat{\tau}_1)}{(\hat{\tau}_1 - \hat{\tau}_2)} e^{-t/\hat{\tau}_1} + \frac{(\hat{\tau}_a - \hat{\tau}_2)}{(\hat{\tau}_2 - \hat{\tau}_1)} e^{-t/\hat{\tau}_2} \quad (4.10)$$

$$\hat{\tau}_1 = 1.80$$
$$\hat{\tau}_2 = 44.05$$
$$\hat{\tau}_a = 16.02$$

Sweat rate static gain and dynamic functions:

$$\hat{f}_{Sweat}(\Delta T, \Delta H, \Delta W; \hat{\beta}) = 4.03 - 0.56 * \Delta T - 0.14 * \Delta W - 0.10 * \Delta H \\ + 0.018 * \Delta T^2 + 0.011 * \Delta T * \Delta H \quad (4.11)$$

$$\hat{g}_{Sweat}(t;\ \hat{\tau}) = \left(1 + \left(\left(\frac{(\hat{\tau}_a - \hat{\tau})}{\hat{\tau}^2}\right)\left(t - \hat{\theta}\right) - 1\right) e^{-(t-\hat{\theta})/\hat{\tau}}\right) \quad (4.12)$$

$$\hat{\theta} = 298.44 - 24.31 * \Delta T + 11.56 * \Delta W \\ + 0.55 * \Delta T^2 - 0.66 * \Delta T * \Delta W$$
$$\hat{\tau} = 43.41$$
$$\hat{\tau}_a = 23.31$$

where the $\Delta T, \Delta \mathrm{H}, \Delta \mathrm{W}$ terms are the input deviation variables from the initial condition; and $\hat{\theta}$ is the dead time parameter, and since it varies over the input space, it is further modeled as a function of the inputs. The next step in this study is to use the DOD and quantitatively measure the effect of reducing the time length of the experimental trials.

4.3.3 OPTIMIZING THE TIME LENGTH OF EXPERIMENTS

As stated earlier, the third and last objective in this study is to reduce the time of each experimental trial without losing significant information in parameter estimation. When developing the H-BEST for the BBD and the DOD in this study, the Wissler computer program simulated values of the two responses every 10 minutes for 360 minutes. The reason for using such a long experimental time was to get close to their steady state levels, and since simulated data are used for this study, the length of the experiment is not a concern. However, a more practical design using human subjects would be benefited by shorter times for the experimental trials.

We will again use the D-optimality criterion to assist in this objective to obtain shorter times for trials. Since the H-BEST solution is a nonlinear function, maximizing the information matrix involves maximizing the $\left|\mathbf{V}^{0\mathrm{T}}\mathbf{V}^{0}\right|$, where $\mathbf{V}^{0}$ is a derivation matrix evaluated at the parameter estimates derived from the seven run design in table 4.2 (see Eqs. 4.9 - 4.12). Before the $\mathbf{V}^{0}$ matrix is constructed, one assumption is made to simplify calculations. We assume that the dynamic parameters are constant. This assumption is based on the fact that the static gain parameters are estimated by using the experimental data sampled towards the end of the experiment. The dynamic parameters, on the other hand, are estimates from the data sampled during the middle of the experiment, when most of the change in the responses occurs. Hence, the static gain parameters will be more influenced than the dynamic parameters when reducing the sampling time of an experiment. Thus, the $\mathbf{V}^0$ matrix will be constructed as shown in Eq. 4.13 below.

$$V^0 = \begin{bmatrix} \frac{\partial y(t)}{\partial \beta_0} & \frac{\partial y(t)}{\partial \beta_1} & \cdot\cdot & \frac{\partial y(t)}{\partial \beta_k} \\ & \cdots & & \\ \frac{\partial y(t)}{\partial \beta_0} & \frac{\partial y(t)}{\partial \beta_1} & \cdot\cdot & \frac{\partial y(t)}{\partial \beta_k} \end{bmatrix} \begin{matrix} \text{Evaluated at } \mathbf{U}_1 \text{ and } t = t_0 \\ \cdots \\ \text{Evaluated at } \mathbf{U}_7 \text{ and } t = t_n \end{matrix} \tag{4.13}$$

where y(t) is the H-BEST solution from the DOD, as given in Eqs. 4.9 - 4.12; **U**(t) is the vector of input deviation variables at time t shown in Table 4.2; $\beta_0,\ldots,\beta_k$ are the static gain parameters for each of the responses, where k = 0, …, 6 for skin temperature and k = 0, .., 5 for sweat rate; and *n* is the number of sample points in each run.

The effect of different lengths of experiemental time on the information matrix, $\left|\mathbf{V}^{0\mathrm{T}}\mathbf{V}^0\right|$, can be investigated for the two responses. However, since the sweat rate response has a much larger lag time than the skin temperature, the sweat rate response will reach steady state much later in each experiment than the skin temperature response. Thus, shortening the design time will have a stronger affect on the estimation of parameters in the model for sweat rate compared to the estimation of parameters in the skin temperature model. A measure of information lost by reducing the experimental time can be calculated according to the D-efficiency in Eq. 4.14. The S-plus version 6.0, Lucent Technologies inc., computer codes for finding the determinant of the information matrices for the two responses are given in Appendices D and E.

$$\eta_{D_i} = \frac{\left(\left| V^{0^T} V^0 \right|_{t_i} / N^p{}_{t_i} \right)^{(1/p)}}{\left(\left| V^{0^T} V^0 \right|_{t_{max}} / N^p{}_{t_{max}} \right)^{(1/p)}} \quad (4.14)$$

where p is the number of parameters in the response models (p = 7 for skin temperature and p = 6 for sweat rate); t_i represents the total experimental time investigated; $t_{max} = 360$ minutes, since this is the maximum allowed run time for the Wissler program; and N is the total sample size used for building the information matrix, i.e., $N = r \times n$, where r is the number of runs ($r = 7$) and n is the number of sampling points for each run. The information ratio from Equation 4.13 for different total experimental time when sampling every 10 minutes is given in Fig. 4.4.

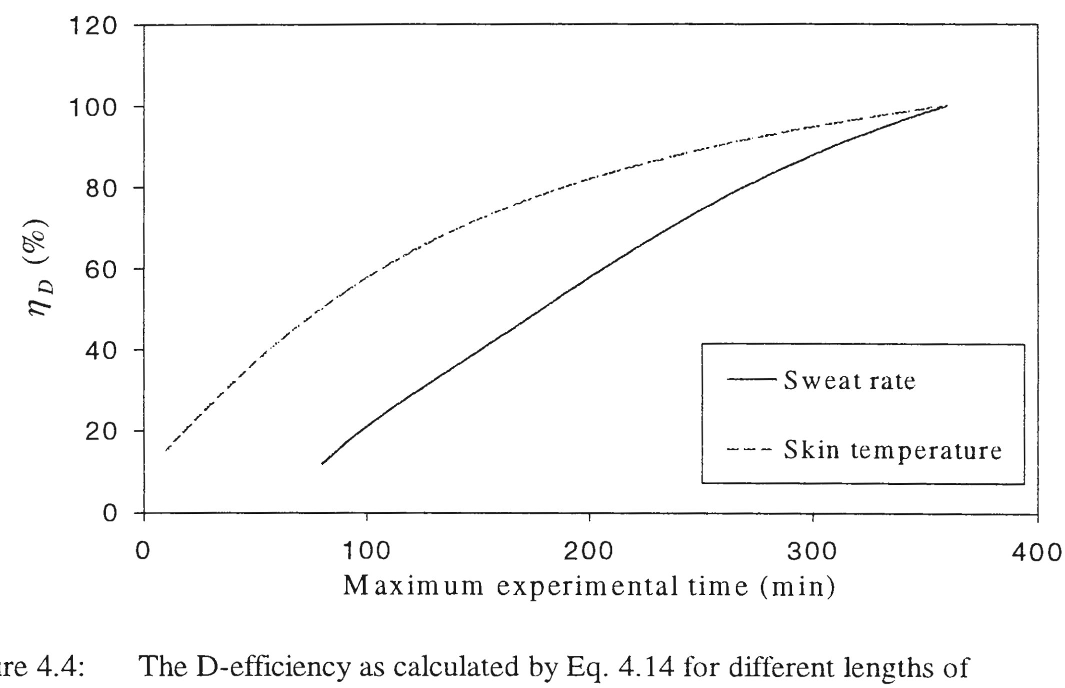

Figure 4.4: The D-efficiency as calculated by Eq. 4.14 for different lengths of experimental times for both the skin temperature response and sweat rate response for a sampling rate of once every 10 minutes.

As stated earlier, the sweat rate response is affected to a greater extent when shortening the length of the experimental trials. That is, in Fig. 4.4 we can see that the D-efficiency for the sweat rate responses decreases faster than the D-efficiency for the skin temperature response, when reducing the experimental times. From Fig. 4.4 we can see conclude that D-efficiency for the skin temperature response decreases slowly for experimental times above about 200 minutes. Hence, the experimental time can be reduced to 210 minutes without significant loss of information and the dynamic parameters are approximately unchanged for experimental times larger than 210 minutes.

The H-BEST models were re-evaluated by running the seven experimental trials from the DOD in Table 4.2 for only 210 minutes instead of 360 minutes, and the dynamic and static parameters were re-estimated using the same procedure as before. Recall that the linear dynamic transfer function used for skin temperature response is a second order overdamped with lead model, and the dynamic transfer function for the sweat rate is a second order critically damped with lead and dead time model. The new H-BEST models developed from for the skin temperature and sweat rate are given in Eqs. 4.15 - 4.16 and Eqs. 4.17 - 4.18, respectively.

<u>Skin temperature static gain and dynamic functions:</u>

$$\begin{aligned}\widehat{f}_{Tskin}(\Delta T,\Delta H,\Delta W;\widehat{\beta}) = 1.26 + 0.26 * \Delta T - 0.018 * \Delta H - 0.18 * \Delta W \\ - 0.0082 * \Delta T^2 + 0.0089 * \Delta T * \Delta W + 0.0017 * \Delta T * \Delta H\end{aligned} \tag{4.15}$$

$$\hat{g}_{Tskin}(t;\hat{\boldsymbol{\tau}}) = 1 + \frac{(\hat{\tau}_a - \hat{\tau}_1)}{(\hat{\tau}_1 - \hat{\tau}_2)} e^{-t/\hat{\tau}_1} + \frac{(\hat{\tau}_a - \hat{\tau}_2)}{(\hat{\tau}_2 - \hat{\tau}_1)} e^{-t/\hat{\tau}_2} \tag{4.16}$$

$$\hat{\tau}_1 = 1.84$$
$$\hat{\tau}_2 = 43.49$$
$$\hat{\tau}_a = 16.21$$

Sweat rate static gain and dynamic functions:

$$\begin{aligned}\hat{f}_{Sweat}(\Delta T, \Delta H, \Delta W; \hat{\boldsymbol{\beta}}) = {} & 3.44 - 0.55 * \Delta T - 0.10 * \Delta W - 0.069 * \Delta H \\ & + 0.022 * \Delta T^2 + 0.0074 * \Delta T * \Delta H\end{aligned} \tag{4.17}$$

$$\hat{g}_{Sweat}(t;\ \hat{\tau}) = \left(1 + \left(\left(\frac{(\hat{\tau}_a - \hat{\tau})}{\hat{\tau}^2}\right)\left(t - \hat{\theta}\right) - 1\right) e^{-(t-\hat{\theta})/\hat{\tau}}\right) \tag{4.18}$$

$$\begin{aligned}\hat{\theta} = {} & 298.44 - 24.31 * \Delta T + 11.56 * \Delta W \\ & + 0.55 * \Delta T^2 - 0.66 * \Delta T * \Delta W\end{aligned}$$
$$\hat{\tau} = 39.27$$
$$\hat{\tau}_a = 18.96$$

where the $\Delta T, \Delta \mathrm{H}, \Delta \mathrm{W}$ terms are the input deviation variables from the initial condition; and $\hat{\theta}$ is the dead time parameter, and since it varies over the input space, it is further modeled as a function of the inputs.

4.4 Results

By using the closed-form H-BEST models in a DOD, the required number of trials for a two-output, three-input system is reduced from 13 experimental trials to 7. The ability of H-BEST to predict the HTS was investigated for a randomly generated input sequence also called the test sequence, as showed in Fig. 4.5. The Fortran code used to simulate the test sequence for the Wissler program is given in Appendix A. The simulated data by

Wissler and the responses predicted by H-BEST obtained from the BBD and the DOD for the skin temperature and sweat rate are given in Figs. 4.6 and 4.7, respectively.

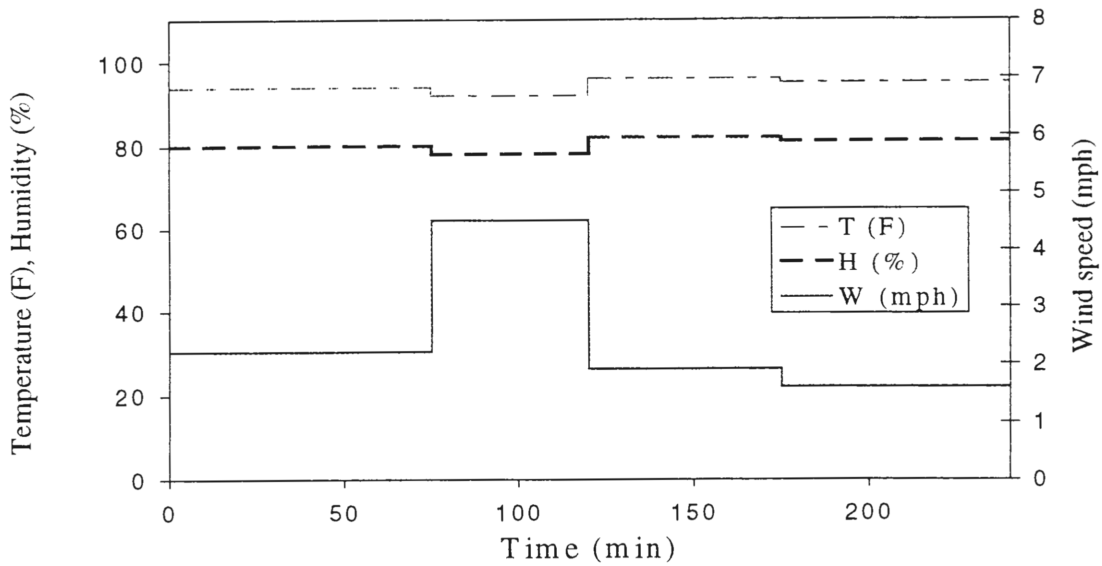

Figure 4.5: The input sequence used for evaluating the H-BEST models obtained from the BBD and DOD.

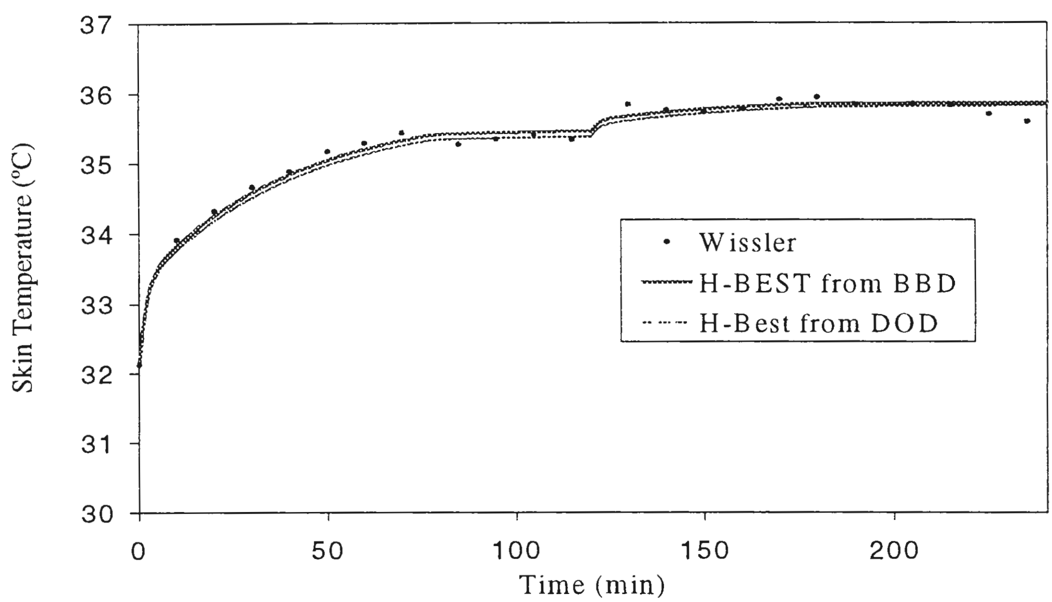

Figure 4.6: The skin temperature response obtained from the Wissler simulation and predicted H-BEST model obtained from the BBD and DOD in Table 4.2 for the test sequence given in Fig. 4.5.

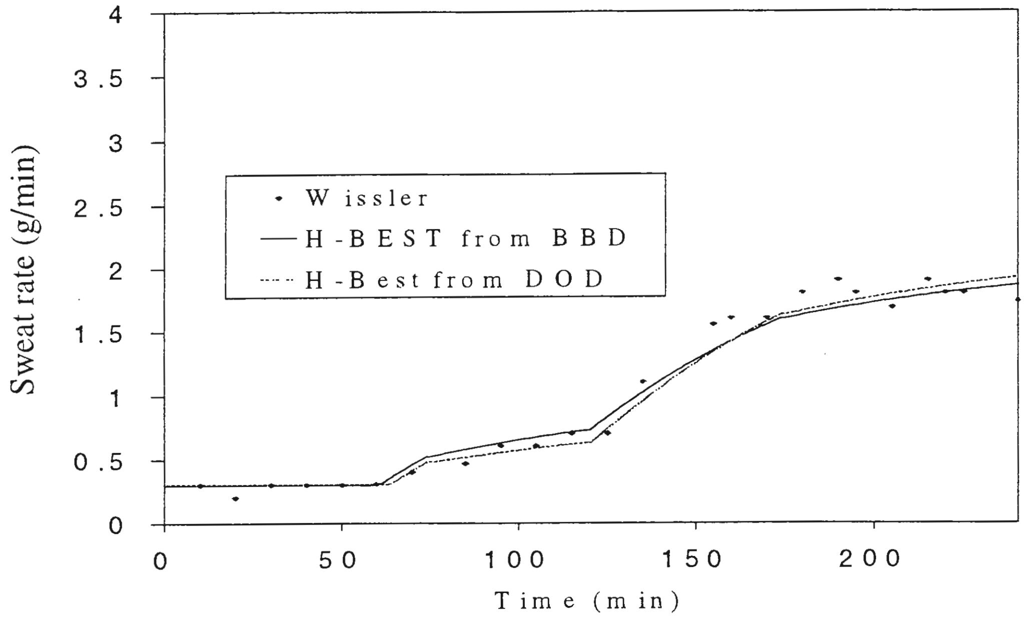

Figure 4.7: The sweat rate response obtained from the Wissler simulation and predicted H-BEST model obtained from the BBD and DOD in Table 4.2 for the test sequence given in Fig 4.5.

The predictions by H-BEST obtained by using the BBD and the DOD agree well with the simulated data. That is, there is no significant deviation between the simulated data and the predicted data. Thus, the predictive models from the DOD with almost half as many experimental trials seem to predict just as well as the predictive models from the BBD. This close agreement is seen in both the output responses.

The second objective was to ascertain if the experimental time for each run could be reduced without losing too much information in the parameter estimates. The H-BEST models derived for the BBD and the DOD were both developed from Wissler simulated data that are sampled every 10 minutes for total experimental time of 360 minutes. The total time of the experiments need to be reduced in order to identify models from data collected when using humans as subjects, instead of simulations. Figs. 4.8 and 4.9 show the output responses from Wissler simulation and predicted responses using H-BEST derived from the DOD in Table 4.2 for an experimental duration of 360 min. (Eqs. 4.9-12) and 210 min (Eqs. 4.15-4.18) for the test sequence shown in Figure 4.5.

The skin temperature predictions by the H-BEST models derived from the DOD in Table 4.2 for the reduced experimental time closely follows the simulated data as showed in Fig. 4.8. In other words, there is no significant difference in the skin temperature predictions from H-BEST for the two different time-lengths of the experiments. The same conclusion can be reached for the sweat rate prediction by looking at Fig. 4.9. That is, the sweat rate prediction from H-BEST for the DOD in Table 4.2 for the reduced experimental length closely follows the simulated data. The generated sweat rate data has a lot of noise in it but H-BEST captures the response very well. Hence, the total experimental time can be significantly reduced without losing critical information needed for estimation of the H-BEST models.

That is, the skin temperature and sweat rate response can be accurately predicted from models obtained using only seven experiments with each a total experimental time of 210 minutes, when sampling the output responses every 10 minutes. This is a great improvement compared to the initial BBD of 13 runs and a total experimental time of 360 minutes for each run, when sampling every 10 minutes.

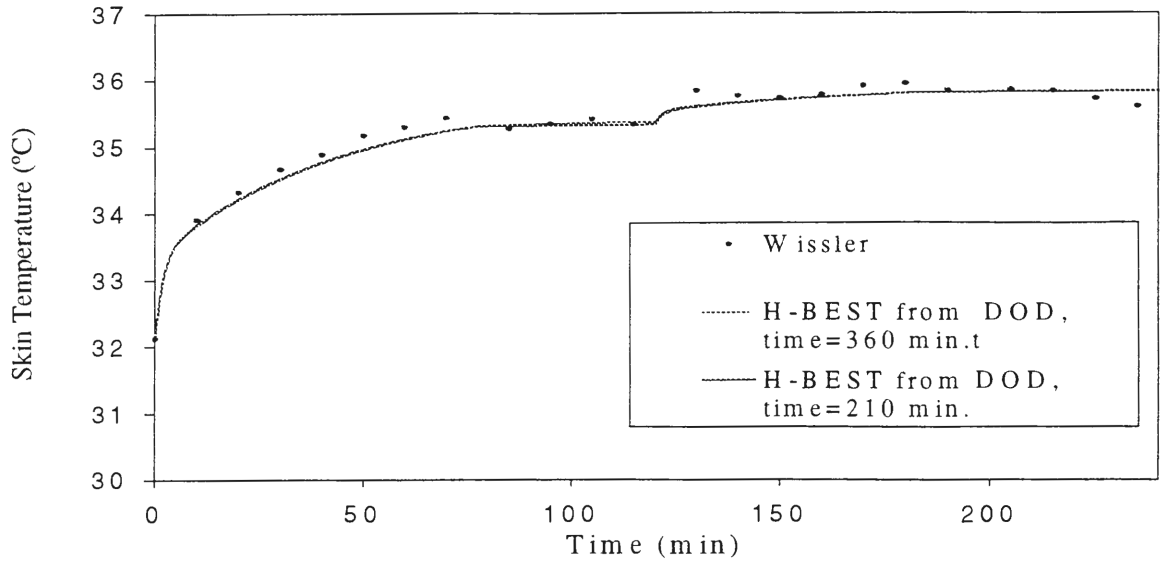

Figure 4.8: The skin temperature response obtained from the Wissler simulation and the H-BEST fitted response obtained from the DOD given in Table 4.2 for experimental lengths of 360 minutes and 210 minutes when sampling every 10 minutes for the test sequence in Figure 4.5.

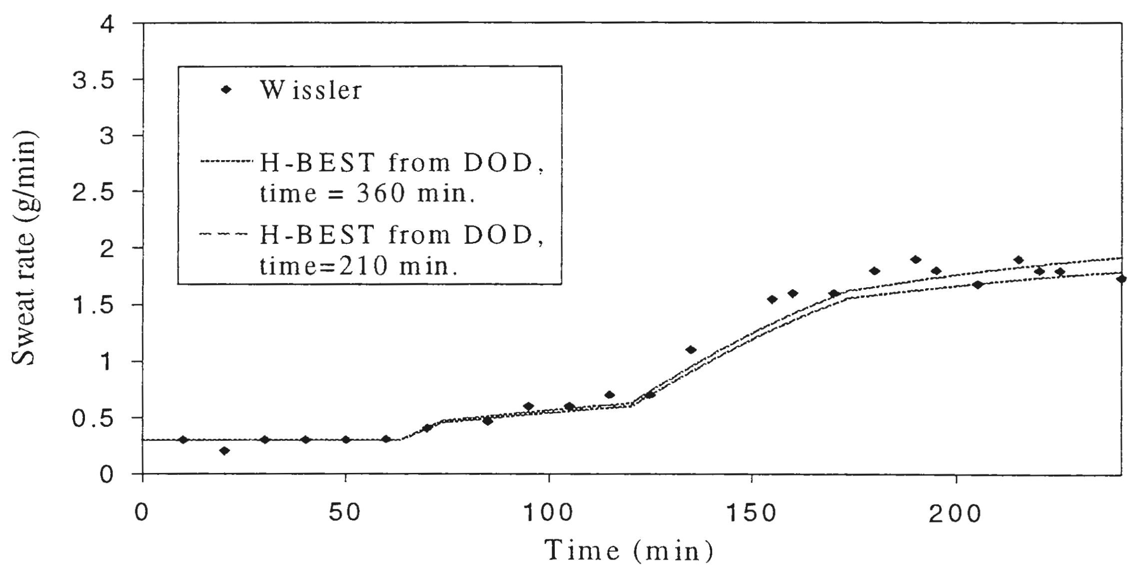

Figure 4.9: The skin temperature response obtained from the Wissler simulation and the H-BEST fitted response obtained from the DOD given in Table 4.2 for experimental lengths of 360 minutes and 210 minutes when sampling every 10 minutes for the test sequence in Figure 4.5.

4.5 Conclusions

The main objective of this study was to develop an accurate optimal dynamic model for the HTS. The skin temperature and sweat rate was generated using the Wissler [19] computer model as a surrogate human under different environmental conditions. The optimization involved minimizing the number of experimental trials as well as reducing the total time of each experiment. Using this methodology, we found an efficient and practical procedure to model HTS using human subjects.

The sweat rate and skin temperature were modeled using a methodology based on a closed-form continuous-time exact solution to a Hammerstein process called H-BEST. The study showed that H-BEST can accurately predict the responses of skin temperature and sweat rate for changes in the environmental temperature, relative humidity, and wind speed, the model identification is achieved from a design with only seven runs and a total experimental time of 210 minutes for each run. The excellent performance of H-BEST follows from the fact that a Hammerstein structure is a good approximation of the HTS as simulated by the Wissler computer program.

There are a few considerations that need to be taken into account when using the proposed modeling approach. First, the lack of a steady state response for the outputs, is a characteristic of the simulator used to generate the data and not of the actual human thermoregulatory process. It is likely that the H-BEST method would predict better for actual experimental data. Secondly, although the model does a reasonably good job of describing individual response over a broad range of conditions, one should extrapolate outside these conditions with care.

Future research would consist of exploring the use of H-BEST for modeling HTS using humans as the experimental subjects. This work has proposed a procedure that gives guidance and insight of such a study. In addition, note that this work focused on the effects of heat and high humidity with low wind speed. Thus, this approach can be applied for other ranges of these input variables, or predict other responses associated with HTS. In addition, in this study we only used step input changes. However, the change in environmental conditions is more often as a ramp function. Thus, future research work should also consists of modeling the HTS with ramp-input change or other types of input changes.

NOMENCLATURE

T = Temperature of the environment
H = Relative Humidity of the environment
W = Wind speed of ambient air
t = time
U = vector of input variables
y = vector of output variables

Greek Letters

β = Vector of parameter estimates of the static gain function of the outputs
τ = Vector of parameter estimates of the dynamic function of the outputs
θ = dead time for the dynamic function of the sweat rate response

Subscripts

Tskin = Skin Temperature
Sweat = Sweat rate

Superscripts

^ = Estimate

Abbreviation

BBD = Box-Behnken Design
DOD = D-optimal Design
H-BEST = Hammerstein Block-oriented Exact Solution Technique
HTS = Human thermoregulatory system
MIMO = Multiple-input, multiple-output
SDOE = Statistical Design of Experiments
SISO = Single-input, single-output

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CHAPTER 5. SUMMARY AND RECOMMENDATIONS FOR FUTURE WORK

5.1. CONCLUSIONS

With the growing industrial demand and interest in exploring space, mankind have started to be exposed to extreme environmental conditions. These extreme environmental conditions can have a serious effect on our health. Thus, the need for understanding how humans respond to these situations has increased. Furthermore, the necessity to develop dynamic models for the human thermoregulation has become of great importance. Historically, there have been mainly two approaches taken to human thermoregulatory modeling. They are the empirical approach and the theoretical approach. However, there are weaknesses in both these approaches. As discussed in this work, an empirical approach restricts modeling to the individual case used for the data collection and requires enormous amount of data to capture transient and ultimate behavior. More importantly, even modeling chemical processes dynamically by using empirical models are not encourage due to the huge data requirement. Another difficulty in dealing with empirical methods is the requirement of constant and frequent sampling rate. Thus, the empirical model does not appear to be practical for modeling dynamical physical or biological behaviors. On the other hand, the weakness of the theoretical model is usually lack of knowledge of the system, which limits the ability to obtain accurate predictive models.

This work utilized a new closed-form continuous-time exact solution to a Hammerstein system, called H-BEST developed by Rollins et al. [5]. The Hammerstein system [1] is a block-oriented system with a nonlinear static gain block followed by a linear dynamic block . Since, H-BEST is an exact solution to Hammerstein it can successfully and accurately predict responses from systems that are Hammerstein or approximately Hammerstein in nature. Most of the Hammerstein methods in literature are discrete-time. However, there are some critical drawbacks to these discrete-time models. These drawbacks are especially important when sampling is infrequent or non-constant. In addition, the modeling identification can be rather extensive due to the large amount of estimated parameters, depending on the sampling rate and number of input variables. There is also limitation in extrapolation when using discrete-time models. As stated earlier, H-BEST is a closed-form continuous-time solution to Hammerstein, and this is the only closed form continuous-time model we have found in literature.

H-BEST has been applied to both simulated and real processes. H-BEST has also been applied successfully to a complex process dynamics and MIMO processes. In a previous study by Walker [6], the H-BEST approach was introduced to the human thermoregulatory system in a SISO study. Walker felt that it had much promise in dynamic modeling of the HTS.

In this thesis H-BEST was used in MIMO modeling of the human thermoregulatory system, by using the Wissler [8] model as the experimental subject. The work successfully developed an accurate and efficient model of the skin temperature and sweat rate for changes in environmental variables. The inputs for this study were the environmental temperature, relative humidity, and wind speed. The efficiency in model identification is based on that the models where developed from an optimal number of experimental trails. That is, as few trials as possible, while still obtaining good estimates of the parameters. There is a great need to be able to develop models from a few numbers of experimental trials. Considering that experiments on human subject can be both costly and inhumane in some situations. In addition, the experimental times for each trial is also considerably reduces, without losing significant information in parameter estimates. Hence, a practical procedure for modeling the human thermoregulatory system with humans as experimental subjects has been developed in this work. In addition, since H-BEST, which is an exact solution to Hammerstein process, accurately modeled the responses, we can conclude that the human thermoregulatory system can be approximated by a Hammerstein system, given that the Wissler program characterizes this behavior adequately.

5.2. FUTURE RESEARCH WORK

Future research would consist in exploring the H-BEST for modeling humans as the experimental subject. Hence, this work has proposed a practical procedure to carry out the experiment on humans. Furthermore, this work focused on the effects of heat and high humidity with low wind speed. Thus, this approach can be applied for other ranges of these input variables, or predict other response variables. In addition, in this study only step input changes were used. However, the changes in environmental conditions are rarely step changes in nature, but rather ramp input changes. Thus, potential future research work would also consist of developing a procedure for modeling the human thermoregulatory system with a ramp input change or other types of inputs. Future research would also consist of applying other block-oriented models than the Hammerstein system, for example Wiener or Sandwich systems. In Wiener systems the linear dynamic block is followed by a nonlinear static gain block, and these system predict very well for processes with high nonlinear dynamics. Sandwich systems are a combination of the Hammerstein and the Wiener, where you have first a linear dynamic block followed by a nonlinear static block and after that a linear dynamic block again. In addition, applying other optimality criteria for designing the experiments should also be investigated. That is, instead of using a D-optimal criterion that focuses on parameter estimation, other criterion that focuses on prediction can be more useful and maybe utilize even better prediction models.

5.3. REFERENCES

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APPENDIX A. FORTRAN COMPUTER CODE USED TO GENERATE THE TEST SEQUENCE FOR THE WISSLER PROGRAM

```
                                   .00000   .00000   .00000
NO
 182.0     12.00000   0.0
  .00  .00  .00  .00  .00  .00  .00  .00  .00  .00  .00  .00  .00  .00  .00
NO
AIR      AIR
YES  NO   NO   YES
       SIMULATION time 0-75
NEW
GAS
  14.69    94.000   86.95    94.0000  2.00000   .00000   .00000
 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00
SIT       2.2000
 285.76     0.00
   .05000   .70000   .10000   .10000
   .12000   .12000
10.00000   1.250  .00278
NUDE NO  3 YES
CTST NO  4 YES
CTTN NO  6 YES
CTST NO  7 YES
CTTN NO  9 YES
CTTN NO  10 YES
CTTN NO  12 YES
CTTN NO  13 YES
CTTN NO  15 YES
  0.00     68.00000  50.0
    SIMULATION time 75-120
NEW
GAS
  14.69    92.000   84.20    92.0000  2.00000   .00000   .00000
 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00
SIT       4.5000
 285.76     0.00
   .05000   .70000   .10000   .10000
   .12000   .12000
10.00000   2.000  .00278
NUDE NO  3 YES
```

```
CTST NO   4 YES
CTTN NO   6 YES
CTST NO   7 YES
CTTN NO   9 YES
CTTN NO  10 YES
CTTN NO  12 YES
CTTN NO  13 YES
CTTN NO  15 YES
  0.00      68.00000  50.0
    SIMULATION time 120-175
NEW
GAS
  14.69     96.000   89.68     96.0000   2.00000    .00000    .00000
 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00
SIT         1.9000
 285.76      0.00
   .05000    .70000    .10000    .10000
   .12000    .12000
 5.00000    3.250   .00278
NUDE NO   3 YES
CTST NO   4 YES
CTTN NO   6 YES
CTST NO   7 YES
CTTN NO   9 YES
CTTN NO  10 YES
CTTN NO  12 YES
CTTN NO  13 YES
CTTN NO  15 YES
  0.00      68.00000  50.0
    SIMULATION time 175-240
NEW
GAS
  14.69     95.000   88.30     95.0000   2.00000    .00000    .00000
 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00
SIT         1.6000
 285.76      0.00
   .05000    .70000    .10000    .10000
   .12000    .12000
 5.00000    4.000   .00278
NUDE NO   3 YES
CTST NO   4 YES
CTTN NO   6 YES
CTST NO   7 YES
```

```
CTTN NO   9 YES
CTTN NO  10 YES
CTTN NO  12 YES
CTTN NO  13 YES
CTTN NO  15 YES
  0.00      68.00000  50.0
FINISH
STOP
```

APPENDIX B. SAS COMPUTER CODE USED TO GENERATE THE D-OPTIMALITY DESIGNS FOR THE TWO RESPONSES

Computer Code:

```
/* This is a program to generate a D-optimal design
Input variables: Relative Humidity (H), Wind speed (W), Temperature (T)*/

/* Response : Mean skin temperature */

Data Input;
        input T W H;
        cards;
        94 3 85                     /* A 3^3 factor design used as the candidate runs */
        94 3 80
        94 3 75
        94 1 85
        94 1 80
        94 1 75
        94 5 85
        94 5 80
        94 5 75
        90 3 85
        90 3 80
        90 3 75
        90 1 85
        90 1 80
        90 1 75
        90 5 85
        90 5 80
        90 5 75
        98 3 85
        98 3 80
        98 3 75
        98 1 85
        98 1 80
        98 1 75
        98 5 85
        98 5 80
        98 5 75
;
Run;


Data Initdesign;
```

```
        input T W H;
        cards;
        94 1 85                          /* Initial guess of the seven runs */
        94 3 80
        98 3 85
        94 1 75
        98 3 75
        90 3 75
        90 3 85
        ;
Run;

Proc Optex data=Input;                          /* procedure that generates a D-   */
  model T H W T*H T*T T*W;                      /* optimal design, with as many   */
  examine design;                               /* runs as the initial guesses,  out */
  generate criterion=D initdesign=Initdesign;   /* of the candidate runs specified */
  output out=designpts;
run;
```

SAS output:

The SAS System
The OPTEX Procedure

Factor Ranges

Factor	Low Value	High Value
T	90.000000	98.000000
H	75.000000	85.000000
W	1.000000	5.000000

The SAS
The OPTEX Procedure

Design Number	D-Efficiency	A-Efficiency	G-Efficiency	Average Prediction Standard Error
1	57.1429	25.0000	60.3023	1.1024

The SAS System
The OPTEX Procedure
Examining Design Number 1

Log determinant of the information matrix	9.7041E+00
Maximum prediction variance over candidates	2.7500
Average prediction variance over candidates	1.2153
Average variance of coefficients	0.5714
D-Efficiency	57.1429
A-Efficiency	25.0000

Point Number	T	H	W
1	90	75	3
2	90	85	1
3	90	85	5
4	94	85	5
5	98	75	3
6	98	85	1
7	98	85	5

<u>Computer Code:</u>

```
/* Response Sweat rate */

Data Input;
        input T W H;
        cards;
        94 3 85                    /* A 3^3 factor design used as the candidate runs */
        94 3 80
        94 3 75
        94 1 85
        94 1 80
        94 1 75
        94 5 85
        94 5 80
        94 5 75
        90 3 85
        90 3 80
        90 3 75
        90 1 85
        90 1 80
        90 1 75
        90 5 85
        90 5 80
        90 5 75
        98 3 85
        98 3 80
        98 3 75
        98 1 85
        98 1 80
        98 1 75
        98 5 85
        98 5 80
        98 5 75
;
Run;

Data Initdesign;
        input T W H;
        cards;
        94 1 85                    /* Initial guess of the six runs */
        94 3 80
        98 3 85
```

```
    94 1 75
    98 3 75
    90 3 75
    90 3 85
    ;
Run;

Proc Optex data=Input coding=none;          /* procedure that generates a D-   */
 model T H W T*H T*T;                       /* optimal design, with as many   */
 examine design;                            /* runs as the initial guesses,  out */
 generate criterion=D initdesign=Initdesign; /* of the candidate runs specified */
 output out=designpts;
run;
```

SAS Output:

The SAS System
The OPTEX Procedure

Factor Ranges

Factor	Low Value	High Value
T	90.000000	98.000000
H	75.000000	85.000000
W	1.000000	5.000000

The SAS System
The OPTEX Procedure

Design Number	D-Efficiency	A-Efficiency	G-Efficiency	Average Prediction Standard Error
1	66.6667	47.0588	89.4427	0.9280

The SAS System
The OPTEX Procedure
Examining Design Number 1

Log determinant of the information matrix	8.3178E+00
Maximum prediction variance over candidates	1.2500
Average prediction variance over	0.8611
Average variance of coefficients	0.3542
D-Efficiency	66.6667
A-Efficiency	47.0588

Point Number	T	H	W
1	90	75	5
2	90	85	1
3	94	75	1
4	94	85	5
5	98	75	5
6	98	85	1

APPENDIX C. S-PLUS CODE USED TO COMPARE THE INFORMATION MATRIXES OF THE SEVEN RUN D-OPTIMAL DESIGN AND THE SIX RUN D-OPTIMAL DESIGN FOR SWEAT RATE.

```
# This code compares the "D-efficiency" for the 7 parameter
# model that is D-optimal to Tskin compared to the
# 6 parameter model that is D-optimal for Sweat rate.

# The D-optimal 7 parameter design for Tskin (design 1)
#   T   H   W
#   90  75  3
#   90  85  1
#   90  85  5
#   94  85  5
#   98  75  3
#   98  85  1
#   98  85  5

#  The D-optimal 6 parameter design for Sweat rate (design 2)
#   T   H   W
#   90  75  5
#   90  85  1
#   94  75  1
#   94  85  5
#   98  75  5
#   98  85  1

# The Log determinant of the information matrix is 8.3178 for design 2.

# To be able to compare the two designs, the determinant of
#  the 6X6 matrix from design 1, when omitting the T*W
#  interaction term, (not significant for modeling the sweat rate).
#  is calculated.

# Building the model matrix from design 1, X,  with the T*W interaction omitted:

X <- matrix(c(1, 1, 1, 1, 1, 1, 1, -1, -1, -1, 0, 1, 1, 1, -1, 1, 1, 1, -1, 1, 1, 0, -1, 1, 1, 0, -1, 1, 1,
    -1, -1, 0, -1, 1, 1, 1, 1, 1,
    0, 1, 1, 1,  ), 7, 6, byrow = F)
```

```
#  Building the X^T X matrix, information matrix
> XtX <- t(X) %*% X

.
# Calculating the determinant of the information matrixes for the two designs
detDesign2 <- exp(8.3178)
detDesign1 <- det(XtX)

# Calculating the D-efficiency as stated in Chapter 4.

p<-6        # Number of parameters

Deff <- ((detDesign1)/(detDesign2))^(1/p)

> 0.9999944
```

APPENDIX D. S-PLUS CODE USED TO CALCULATE THE DETERMINANT OF THE NONLINEAR INFORMATION MATRIX FOR SKIN TEMPERATURE RESPONSE

```
# This program is use calculate the determinant of the information matrix
#************************************************************
# Inputs: Temperature (dT), Relative Humidity (dH), Wind speed (dW)
# Response: Skin Temperature
# H-Best = f(dH,dT,dW)*g(t)
# g(t) - 2nd order overdamped with lead
#************************************************************
# Reading the initial values for parameters

# run 1: T=90 F H=75% W=3 mph dT=10 dH=25 dW=0
# run 2: T=90 F H=85% W=1 mph dT=10 dH=35 dW=-2
# run 3: T=90 F H=85% W=5 mph dT=10 dH=35 dW=2
# run 4: T=94 F H=85% W=5 mph dT=14 dH=35 dW=2
# run 5: T=98 F H=75% W=3 mph dT=18 dH=25 dW=0
# run 6: T=98 F H=85% W=1 mph dT=18 dH=35 dW=-2
# run 7: T=98 F H=85% W=5 mph dT=18 dH=35 dW=2

# Input vectors with the deviation values of the seven runs
dT<-c(10,10,10,14,18,18,18)
dH<-c(25,35,35,35,25,35,35)
dW<-c(0,-2,2,2,0,-2,2)

# Estimates of the dynamic parameters
tau1<-1.800313
tau2<-44.0513
taua<-16.02332

# Estimate of the steady State gain parameters
b0<-1.1616875
b1<-0.2659938
b2<--0.09625
b3<--0.007837
b4<--0.007606
b5<-0.003625
b6<-0.0009637


# The time vector, sampling every 10 minutes
```

```
t<-c(10,20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200,
    210, 220, 230, 240)

#Calculating the gain and dynamic functions
f<-b0+b1*dT+b2*dW+b3*dH+b4*(dT)^2+b5*dT*dW+b6*dT*dH
g<-(1+(taua-tau1)/(tau1-tau2)*exp(-1*(t/tau1))+(taua-tau2)/(tau2-tau1)*exp(-1*(t/tau2)))

#Calculating the partial derivatives for each of the seven runs
dydb01<-g
dydb11<-dT[1]*g                # run 1
dydb21<-dW[1]*g
dydb31<-dH[1]*g
dydb41<-dT[1]^2*g
dydb51<-dT[1]*dW[1]*g
dydb61<-dT[1]*dH[1]*g


dydb02<-g
dydb12<-dT[2]*g                # run 2
dydb22<-dW[2]*g
dydb32<-dH[2]*g
dydb42<-dT[2]^2*g
dydb52<-dT[2]*dW[2]*g
dydb62<-dT[2]*dH[2]*g


dydb03<-g
dydb13<-dT[3]*g                #run 3
dydb23<-dW[3]*g
dydb33<-dH[3]*g
dydb43<-dT[3]^2*g
dydb53<-dT[3]*dW[3]*g
dydb63<-dT[3]*dH[3]*g


dydb04<-g
dydb14<-dT[4]*g                 # run 4
dydb24<-dW[4]*g
dydb34<-dH[4]*g
dydb44<-dT[4]^2*g
dydb54<-dT[4]*dW[4]*g
dydb64<-dT[4]*dH[4]*g


dydb05<-g
```

```
dydb15<-dT[5]*g                # run 5
dydb25<-dW[5]*g
dydb35<-dH[5]*g
dydb45<-dT[5]^2*g
dydb55<-dT[5]*dW[5]*g
dydb65<-dT[5]*dH[5]*g


dydb06<-g
dydb16<-dT[6]*g                # run 6
dydb26<-dW[6]*g
dydb36<-dH[6]*g
dydb46<-dT[6]^2*g
dydb56<-dT[6]*dW[6]*g
dydb66<-dT[6]*dH[6]*g


dydb07<-g
dydb17<-dT[7]*g                # run 7
dydb27<-dW[7]*g
dydb37<-dH[7]*g
dydb47<-dT[7]^2*g
dydb57<-dT[7]*dW[7]*g
dydb67<-dT[7]*dH[7]*g

# Build the information matrix, binding the partial derivatives together
u1<-cbind(dydb01,dydb11,dydb21,dydb31,dydb41,dydb51,dydb61)
u2<-cbind(dydb02,dydb12,dydb22,dydb32,dydb42,dydb52,dydb62)
u3<-cbind(dydb03,dydb13,dydb23,dydb33,dydb43,dydb53,dydb63)
u4<-cbind(dydb04,dydb14,dydb24,dydb34,dydb44,dydb54,dydb64)
u5<-cbind(dydb05,dydb15,dydb25,dydb35,dydb45,dydb55,dydb65)
u6<-cbind(dydb06,dydb16,dydb26,dydb36,dydb46,dydb56,dydb66)
u7<-cbind(dydb07,dydb17,dydb27,dydb37,dydb47,dydb57,dydb67)


V<-rbind(u1,u2,u3,u4,u5,u6,u7)

VtV<-t(V)%*%V

#Calculating the Determinant
DetVtV<-det(VtV)
DetVtV
```

APPENDIX E. S-PLUS CODE USED TO CALCULATE THE DETERMINANT OF THE NONLINEAR INFORMATION MATRIX FOR SWEAT RATE RESPONSE

```
# This program is use to calculate the determinant of the information matrix
# Inputs: Temperature (dT), Relative Humidity (dH), Wind speed (dW)
#  H-Best = f(dH,dT,dW)*g(t)
#************************************************************
# Response: Sweat rate
# g(t) - 2nd order Critically damped with lead and dead time
#***********************************************************
# Reading the initial values for parameters

# run 1: T=90 F H=75% W=3 mph dT=10 dH=25 dW=0
# run 2: T=90 F H=85% W=1 mph dT=10 dH=35 dW=-2
# run 3: T=90 F H=85% W=5 mph dT=10 dH=35 dW=2
# run 4: T=94 F H=85% W=5 mph dT=14 dH=35 dW=2
# run 5: T=98 F H=75% W=3 mph dT=18 dH=25 dW=0
# run 6: T=98 F H=85% W=1 mph dT=18 dH=35 dW=-2
# run 7: T=98 F H=85% W=5 mph dT=18 dH=35 dW=2

#Input vectors of the deviation values for the seven runs
dT<-c(10,10,10,14,18,18,18)
dH<-c(25,35,35,35,25,35,35)
dW<-c(0,-2,2,2,0,-2,2)

# Estimates of the dynamic parameters
tau<-43.414
taua<-23.3137
theta<-(298.4375-24.3125*dT+11.5625*dW+0.546875*(dT)^2-0.65625*dT*dW)

# Estimate for the Steady State gain parameters
b0<-4.03125
b1<--0.556875
b2<--0.1425
b3<--0.10375
b4<-0.018125
b5<-0.010875
```

```
# The time vector, when sampling every 10 minutes
t<-c(10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190,200,
    210, 220, 230, 240 )

#Calculating the gain and dynamic functions
f<-b0+b1*dT+b2*dW+b3*dH+b4*(dT)^2+b5*dT*dH
g1<-(1+((taua-tau)/(tau)^2*(t-theta[1])-1)*exp(-(t-theta[1])/tau))
g2<-(1+((taua-tau)/(tau)^2*(t-theta[2])-1)*exp(-(t-theta[2])/tau))
g3<-(1+((taua-tau)/(tau)^2*(t-theta[3])-1)*exp(-(t-theta[3])/tau))
g4<-(1+((taua-tau)/(tau)^2*(t-theta[4])-1)*exp(-(t-theta[4])/tau))
g5<-(1+((taua-tau)/(tau)^2*(t-theta[5])-1)*exp(-(t-theta[5])/tau))
g6<-(1+((taua-tau)/(tau)^2*(t-theta[6])-1)*exp(-(t-theta[6])/tau))
g7<-(1+((taua-tau)/(tau)^2*(t-theta[7])-1)*exp(-(t-theta[7])/tau))

# Setting the dynamic function, g(t) = 0 for times smaller than the dead time, theta
for (i in 1:n){
if (g1[i]<0)  {g1[i]<-0} }

for (i in 1:n){
if (g2[i]<0)  {g2[i]<-0} }

for (i in 1:n){
if (g3[i]<0)  {g3[i]<-0} }

for (i in 1:n){
if (g4[i]<0)  {g4[i]<-0} }

for (i in 1:n){
if (g5[i]<0)  {g5[i]<-0} }

for (i in 1:n){
if (g6[i]<0)  {g6[i]<-0} }

for (i in 1:n){
if (g7[i]<0)  {g7[i]<-0} }


#Calculating the partial derivatives for the seven runs
dydb01<-g1
dydb11<-dT[1]*g1                    # run 1
dydb21<-dW[1]*g1
dydb31<-dH[1]*g1
dydb41<-dT[1]^2*g1
dydb51<-dT[1]*dH[1]*g1
```

```
dydb02<-g2
dydb12<-dT[2]*g2                    # run 2
dydb22<-dW[2]*g2
dydb32<-dH[2]*g2
dydb42<-dT[2]^2*g2
dydb52<-dT[2]*dH[2]*g2


dydb03<-g3
dydb13<-dT[3]*g3                    # run 3
dydb23<-dW[3]*g3
dydb33<-dH[3]*g3
dydb43<-dT[3]^2*g3
dydb53<-dT[3]*dH[3]*g3


dydb04<-g4
dydb14<-dT[4]*g4                    # run 4
dydb24<-dW[4]*g4
dydb34<-dH[4]*g4
dydb44<-dT[4]^2*g4
dydb54<-dT[4]*dH[4]*g4


dydb05<-g5
dydb15<-dT[5]*g5                    # run 5
dydb25<-dW[5]*g5
dydb35<-dH[5]*g5
dydb45<-dT[5]^2*g5
dydb55<-dT[5]*dH[5]*g5


dydb06<-g6
dydb16<-dT[6]*g6                    # run 6
dydb26<-dW[6]*g6
dydb36<-dH[6]*g6
dydb46<-dT[6]^2*g6
dydb56<-dT[6]*dH[6]*g6


dydb07<-g7
dydb17<-dT[7]*g7                    # run 7
dydb27<-dW[7]*g7
dydb37<-dH[7]*g7
dydb47<-dT[7]^2*g7
```

```
dydb57<-dT[7]*dH[7]*g7

# Build the information matrix, binding the partial derivatives together
u1<-cbind(dydb01,dydb11,dydb21,dydb31,dydb41,dydb51)
u2<-cbind(dydb02,dydb12,dydb22,dydb32,dydb42,dydb52)
u3<-cbind(dydb03,dydb13,dydb23,dydb33,dydb43,dydb53)
u4<-cbind(dydb04,dydb14,dydb24,dydb34,dydb44,dydb54)
u5<-cbind(dydb05,dydb15,dydb25,dydb35,dydb45,dydb55)
u6<-cbind(dydb06,dydb16,dydb26,dydb36,dydb46,dydb56)
u7<-cbind(dydb07,dydb17,dydb27,dydb37,dydb47,dydb57)


V<-rbind(u1,u2,u3,u4,u5,u6,u7)
VtV<-t(V)%*%V

#Calculating the Determinant of the information matrix
DetVtV<-det(VtV)

DetVtV
```

ACKNOWLEDGEMENT

I would like to express my gratitude to my academic advisor Dr. Rollins, and my committee members Dr. Morris and Dr. Seagrave. I very much appreciate all of their time and effort in helping me to complete this work. I especially want to extend my thanks to Dr. Rollins for being a mentor, advisor, teacher and also a friend. I also would like to thank all group members and classmates at ISU for their assistance and friendship, especially Nidhi Bhandari for all your help and guidance in writing this thesis.

I wish to thank all the scholarships and grants that made it possible to complete my studies and research in the US. I would like to thank The American-Scandinavian Foundation Grant 2001/2002, Sweden-American Foundation Grant 2001/2002, Henrik Göransson i Sandviken scholarship, Fredrika Bremer scholarship, Adda Dahls scholarship, Anna Withlock scholarship, Stenhagens fond scholarship, Dr. Neuberghs scholarship, T. M. Wallenberg scholarship and the International exchange student scholarship from the Royal Institute of Technology.